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RISK FACTORS ASSOCIATED WITH THE TRANSMISSION OF ANDEAN CUTANEOUS LEISHMANIASIS

Thesis submitted for the degree of Doctor of Philosophy in the University of London

by

Elmer Alejandro LLanos Cuentas, MD, MSc, DrMed

Vector Biology and Epidemiology Unit
Department of Medical Parasitology
London School of Hygiene and Tropical Medicine
University of London

Instituto de Medicine Tropical "Alexander von Humboldt"
y Departamento de Medicina
Universidad Peruana Cayetano Heredia
Lima, Peru

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ABSTRACT

This is a population-based case-control study of the risk factors associated with the transmission of Andean cutaneous leishmaniasis (uta) with a concurrent design comparing persons who developed uta against persons who did not. Cases and controls were matched by age, sex and place of residence. The unit of analysis was the person. The main exposure groups were: characteristics of the house, environmental characteristics around the house, and behaviour patterns of people. The study was carried out in five endemic regions of Peru. 187 cases and 335 controls were admitted to the study. Using matched and conditional logistic regression, in study areas of Lima & Ancash (region 1) and Piura (region 2) Departments we have identified risk factors which imply that transmission occurs (a) inside houses, (b) outside but close to houses, (c) around houses, but not clearly indoors or outdoors, and (d) away from houses. In region 1 we found three risk factors of type a, using a kerosene lamp (OR=6.6, c.i.:2.2-19.7), having a chimney (OR=4.9, c.i.:1.9-12.5) and living in a stone house (OR=2.9, c.i.:1.6-5.2), one of type b, cutting wood (OR=7.4, c.i.:2.1-26.4), and three of type c, living in a house > 30 m from road (OR=3.9, c.i.:1.4-10.7), with a vegetable garden (OR=2.8, c.i.:1.1-4.1) and living in a house having > 6 persons (OR=4.2, c.i.:1.9-9.7). In region 2, we found four risk factors of type c, living in a house having an earth floor (OR=2.3, c.i.:1.1-4.7), with cows (OR=1.3, c.i.:1.1-1.6) and a neighbouring vegetable garden nearby (OR=2.9, c.i.:1.3-6.9), and living > 30 m from a river (OR=3.3, c.i.:3.1-8.4), and one of type d, doing irrigation work at night (OR=2.2, c.i.:1.2-4.2). The variability of risk factors between regions 1 and 2 can be explained by differences in (i) the frequency of exposures and (ii) the importance of factors. We conclude from OR's and PAR's that much transmission occurs around houses. Certainly, some transmission is indoors: the population attributable risk for factors associated with indoor transmission in region 1 was 79%, suggesting the possibility of uta control by preventing biting in houses. It remains questionable how much transmission goes on outdoors.

RESUMEN

Este es un estudio caso-control basado en la población, sobre factores de riesgo asociados con la transmisión de leishmaniasis cutánea Andina (uta). El diseño fue concurrente en el que se comparó personas que desarrollaron uta contra las que permanecieron libres de enfermedad. Los casos y controles fueron pareados por edad, sexo y lugar de residencia. La unidad de análisis fue persona-semestre. Los principales factores de exposición fueron: características de la casa, ambientales alrededor de la casa y patrones de comportamiento de habitantes de las áreas endémicas. Este estudio se realizó en 5 regiones endémicas de uta del Perú, localizas en los Departamentos de Lima + Ancash (región 1) y Piura (región 2), habiéndose admitiendo 187 casos y 335 controles. Utilizando análisis pareado y regresión logística condicional, nosotros identificamos diferentes factores de riesgo que implican que la transmisión de uta ocurre en (a) dentro de las casas, (b) fuera pero alrededor de las casas, (c) en el ambiente doméstico, pero no claramente definido si es dentro o fuera de las casas, y (d) en el área rural. En la región 1 se encontró tres factores de riesgo del tipo a, uso de lámpara de kerosene (OR=6.6, c.i.:2.2-19.7), tener chimenea (OR=4.9, c.i.:1.9-12.5) y vivir en casa con paredes de piedra (OR=2.9, c.i.:1.6-5.2), uno del tipo b, recolectar leña (OR=7.4, c.i.:2.1-26.4), y tres del tipo c, vivir en una casa localizada > 30 m de la carretera (OR=3.9, c.i.:1.4-10.7), con jardín (OR=2.8, c.i.:1.1-4.1) y vivir en una casa que tenga > 6 personas (OR=4.2, c.i.:1.9-9.7). En la región 2, encontramos cuatro factores de riesgo del tipo c, vivir en una casa con piso de tierra (OR=2.3, c.i.:1.1-4.7), con ganado vacuno alrededor de la casa (OR=1.3, c.i.:1.1-1.6), tener vecino (s) con jardín en su casa (OR=2.9, c.i.:1.3-6.9), y vivir > 30 m del río (OR=3.3, c.i.:3.1-8.4); y un factor del tipo d, trabajar en irrigación en las noches (OR=2.2, c.i.:1.2-4.2). La variabilidad de los factores de riesgo entre las regiones 1 y 2 se pueden explicar por diferencias en: (i) frecuencia en las variables de exposición y (ii) de la importancia de los factores. Nosotros concluímos que la mayor parte de la transmisión ocurre alrededor del domicilio. Existe certeza que una parte de ella ocurre al interior de las casas. El cálculo de la población atribuible a riesgo, para los factores asociados con transmisión dentro de las casas fue 79%, lo cual permitiría la utilización de medidas que prevengan la picadura de los insectos en este lugar. Es discutible la proporción de transmisión que ocurre en la área rural.

PREFACE

The mission of the Universities is not to passively transmit knowledge and to prepare professionals. They must constitute active research centers, and participate in the incessant search for truth and in the solution of the many questions that limit the progress of science. This effort is not apart from that of teaching; on the contrary, it raises its quality and allows the students to receive from their instructors the incentive of unanswered questions, and the challenge of unexplained phenomena. Moreover, in general, research is perhaps the most important contribution that Universities may offer to the development progress of the country they belong to.

Extract from the Address of the Rector, Professor Alberto Hurtado (1901-1983), on the occasion of the inauguration of the new building of the Universidad Peruana Cayetano Heredia 1968

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CHAPTER I: INTRODUCTION

The leishmaniases are a group of parasitic diseases with a wide range of clinical manifestations (cutaneous, mucocutaneous, diffuse cutaneous, visceral). In the New World at least 12 species of *Leishmania* are pathogenic for humans (Desjeux 1992, Young & Arias 1992); 88 from more than 350 species or subspecies of sandflies of the genus *Lutzomyia* are proven or suspected vectors of human leishmaniasis and 31 species of mammals are proven or suspected reservoirs (Young & Arias 1992).

Leishmaniasis is a disease that is growing in incidence and public health importance (Desjeux 1992), with an estimated worldwide annual incidence of 400,000 clinical cases, an overall prevalence of 12 million cases and an estimated population at risk of about 367 millions (WHO 1990, Ashford *et al.* 1992); however these amounts probably represent underestimates of the real numbers (Desjeux 1992, Ashford *et al.* 1992).

A. Critical review of case-control studies in leishmaniasis

The contribution of descriptive epidemiology to the scientific knowledge of New World leishmaniasis (NWL) is indisputable. Detailed reviews on parasitological (Lainson & Shaw 1979, 1987, Grimaldi *et al.* 1989), ecological (Lainson & Shaw 1978, Shaw & Lainson 1987), entomological (Young & Arias 1992), immunopathological (Grimaldi 1982, Carvalho *et al.* 1985, Barral-Netto *et al.* 1986), clinical (Marsden 1986, Walton 1987), therapeutic (Marsden 1985, Bryceson 1987, Berman 1988) and public health (Marsden 1984, Walton 1988, Desjeux 1992) aspects of NWL have been published.

The majority of these studies have been observational in nature, permitting the collection of important information and the estimation of certain features of epidemiology of NWL. For instance, we know a good deal about vectors, reservoirs and other components of the cycle of transmission in leishmaniasis. But, this knowledge has not changed the approach of intervention programs. Governmental institutions in Latin-America are using the same methodologies now as in the 1950's and 1960's.

Analytic research in Latin America concerning causality, such as pathogenic mechanism (Saravia *et al.* 1990), diagnosis (Navin *et al.* 1990), rate of conversion to mucosal disease (Campos 1990), and transmission (Rojas 1992, Weigle *et al.* 1992, Llanos-Cuentas & Davies 1992) has grown during the last few years. However, questions such as where and when transmission occurs and how epidemiology relates to entomological parameters have not been addressed in the majority of endemic areas in the New World. These issues are potentially some of the most relevant for choosing an appropriate control strategy.

Only a few studies of risk factors for NWL were published during the 1980's. Some of them (Llanos-Cuentas *et al.* 1984, Tavares *et al.* 1986) assessed the correlation of severity of the primary cutaneous leishmaniasis (CL) with the risk of developing a mucosal lesion, a hypothesis that has been suggested by Dr. Samuel B. Pessôa (Pessôa & Barretto 1948), and proposed more explicitly with the evidence of data from Tres Braços, Brazil (Llanos-Cuentas *et al.* 1984). On the whole, these studies have not been performed systematically with adjustment for multifactorial determinants (confounders, interactions) or bias considerations, though Campos (1990) has recently studied risk factors for development of mucosal lesions using a non-matched case-control design in the Southeast of Peru.

In the International Workshop on Research on Control Strategies for the Leishmaniasis held in Ottawa, Canada, June 1987, Rojas *et al.* (1988) presented the results of a pilot study of risk factors associated with CL caused by *L.panamensis* in Acosta, Costa Rica. A bivariate analysis, controlling for number of inhabitants members of houses (18 cases and 23 controls) selected 7 potential risk factors. Based on this experience a larger study was carried out in the same place (Rojas 1992). This was a population case-control study, with the house as the unit of interest. Controls were children (< 10 years old) in the same age range (+/- 2 years), and located within a radius of +/- 150 meters from the case. An interim analysis using multivariate logistic regression with 29 cases and 76 controls showed the following as potential risk factors: animals under the house (OR=3.6, c.i.: 2.1-5.0), pigs around the house (OR=2.9, c.i.: 1.9-4.0), lack of garbage disposal (OR=2.6, c.i.: 1.2-4.1), inhabitants per house (OR=2.2, c.i.: 1.0-3.4), presence of latrines (OR=2.0, c.i.: 0.6-3.5), and hen-houses (OR=0.7, c.i.: 0.3-2.4). The majority (5/7) of risk factors detected in the pilot study were not selected for the model, but others were added. This emphasized the importance of using a multivariate analysis that was able to control for the effects of other variables that were not controlled for in the bivariate analysis. In addition, relatively small sample size in the latter evaluation could have lead the exclusion of some significant factors. The main factors detected in the final analysis (Rojas-Ocampo 1993), which included 54 cases and 125 controls, were: dogs sleeping around houses at night (OR=2.9, c.i: 1.0-8.1), pigs around the house during daytime (OR=2.1, c.i.:1.1-4.3), domestic animals sleeping or staying under the house at any time (OR=1.8, c.i.: 0.9-3.6), houses with a cement floor (OR=0.5, c.i.: 0.2-1.0). In addition, entomological evaluation in a sub-sample of case-houses and control-houses suggested *Lutzomyia ylephiletor* as the suspected vector in Acosta. So, the risk factors detected suggested intra- and peridomiciliary transmission in a country where traditionally transmission has been considered to occur as an occupational hazard in the forest.

Another well-designed case-control study was carried out in Tumaco, Department of Mariño, Colombia (Weigle *et al.* 1992). The objective was identify and measure risk factors for acquiring infection and disease in a defined rural population that lived in an endemic area where two species of *Leishmania* coexist, *L. panamensis* and *L. braziliensis*, predominantly the former. This was a nested case-control study and the unit of interest was the person. The authors chose a prospective design in order to avoid recall bias and to examine separately risk factors for infections, measured by Montenegro skin test (MST) conversion, and for disease, measured by the development of active cutaneous lesions. Controls for both infections and clinical cases were persons without lesions and who where MST negative at end of the study. The strength of the associations was estimated by the odds ratio, and variables likely to be associated with the case control status ($p < 0.15$) were evaluated in logistic regression models which controlled for age and sex. 227 cases and 227 controls were evaluated in the infection study, and 34 cases and 102 controls for CL study. Risk factors for infection were: occupational, such as farming (OR=2.8, c.i.: 1.5-5.2), hunting (OR=2.4, ci.: 1.2-4.9), lumbering (OR=2.4, c.i.: 1.0-5.7) and fishing (OR=1.6, c.i.: 1.0-2.7), and/or behavioural exposure to the forest, such as entering the forest after sunset (OR=13.3, c.i.: 3.3-51.2), entering the forest but not after sunset (OR = 6.8, c.i.: 1.9-23.3). The risk was greater for males (OR = 23.3, c.i.: 12.2-44.7) and closely dependent the number of hours spent there. In this area infection was more common than disease with an overall ratio of 10:1 (Weigle *et al.* 1992). This is a surprising ratio and suggests either cross-reaction, or that a proportion of parasites are avirulent (Dye & Davies 1990). Risk factors for leishmanial lesions resembled those detected for infection. Thus, the main transmission pattern in Tumaco area was in the forest outside the houses. Determinants of domestic transmission could not be studied because insecticide had been sprayed by the Colombian Malaria Eradication Service in 94% of households. However, the presence of large trees, or trees with exposed roots near to residences moderately increased the risk of infection but not disease.

The case-control method has recently been applied during an outbreak of CL caused by *L. infantum* in Nazareth, Costa Rica (Van der Linden *et al.* submitted). The study comprised 20 case houses and 20 control houses. Significant associations (using logistic regression analysis) were found with dogs living inside the houses, time living in the area and number of people living in the house.

Briefly, we will comment on some other studies on leishmaniasis published during the last five years which have referred to risk factors obtained through positive associations, in order that some of these results could provide a hypothesis for future analytic studies.

In the Latin American literature several factors have been associated with high risk of transmission of leishmaniasis. As already mentioned, the majority of them have been detected on the basis of statistical association, but without representativeness considerations (sample size) and/or not adjusted for multifactorial determinants. Occupation has been the factor most extensively associated with a higher risk of acquiring leishmaniasis, when people were exposured to the sylvatic cycle of the *L. braziliensis* complex (Takafuji *et al.* 1980, Castro 1986, Lumbreras & Guerra 1985). These job activities included deforestation (i.e. farming, road building), extraction of natural products (i.e. oil, wild rubber, timber), hunting or exploring. Further, age (young adults), sex (male) and low socioeconomic status are factors closely related to these jobs in jungle areas of Brazil and Peru (Pessôa & Barretto 1948, Castro 1986, Bartolini *et al.* 1988). Also, in the Mexican State of Campeche (Peninsula of Yucatan), adult males (> 15 years old) entering the forest have been found to be at high risk of disease due to *L. mexicana* (Andrade-Narvaez *et al.* 1992). The location of a house has also been related to increased risk of disease: inhabitants of houses situated close to tropical Atlantic forest in some States of Brazil have suffered high incidences of CL (Castro 1986, Netto *et al.* 1986). Similarly, houses near to the periphery of a village have been associated with more CL in Colombia (Loyola *et al.* 1985).

In the Old Word literature, two studies of risk factors for leishmaniasis have appeared during the last five years. In Alexandria Governorate, Egypt, two case-control studies were done in order to assess risk factors related to transmission in dwellings (Faris *et al.* 1988). The first used cases of infantile visceral leishmaniasis (VL) proven parasitologically positive. The second used serologically positive subjects who were identified through a survey, as well as the clinically evident cases. The unit of analysis in both studies was the house and cases and controls were matched by age (children under 5 years old) and place of residence (nearby household). In the former, households with VL cases were more likely to store garbage in open containers. In the serological study both VL cases and seropositive individuals tended to live in houses facing open areas in which garbage was stored. However, these results have two limitations: (i) the analysis was made using only simple chi square tests; a matching design must be accompanied by matched analysis, otherwise the validity of comparison is reduced (Schlesselman 1982), (ii) small sample sizes (12 cases of VL and 22 seropositivity cases) leading wide confidence intervals. Thus, these results are statistically questionable, but they could be biologically significant.

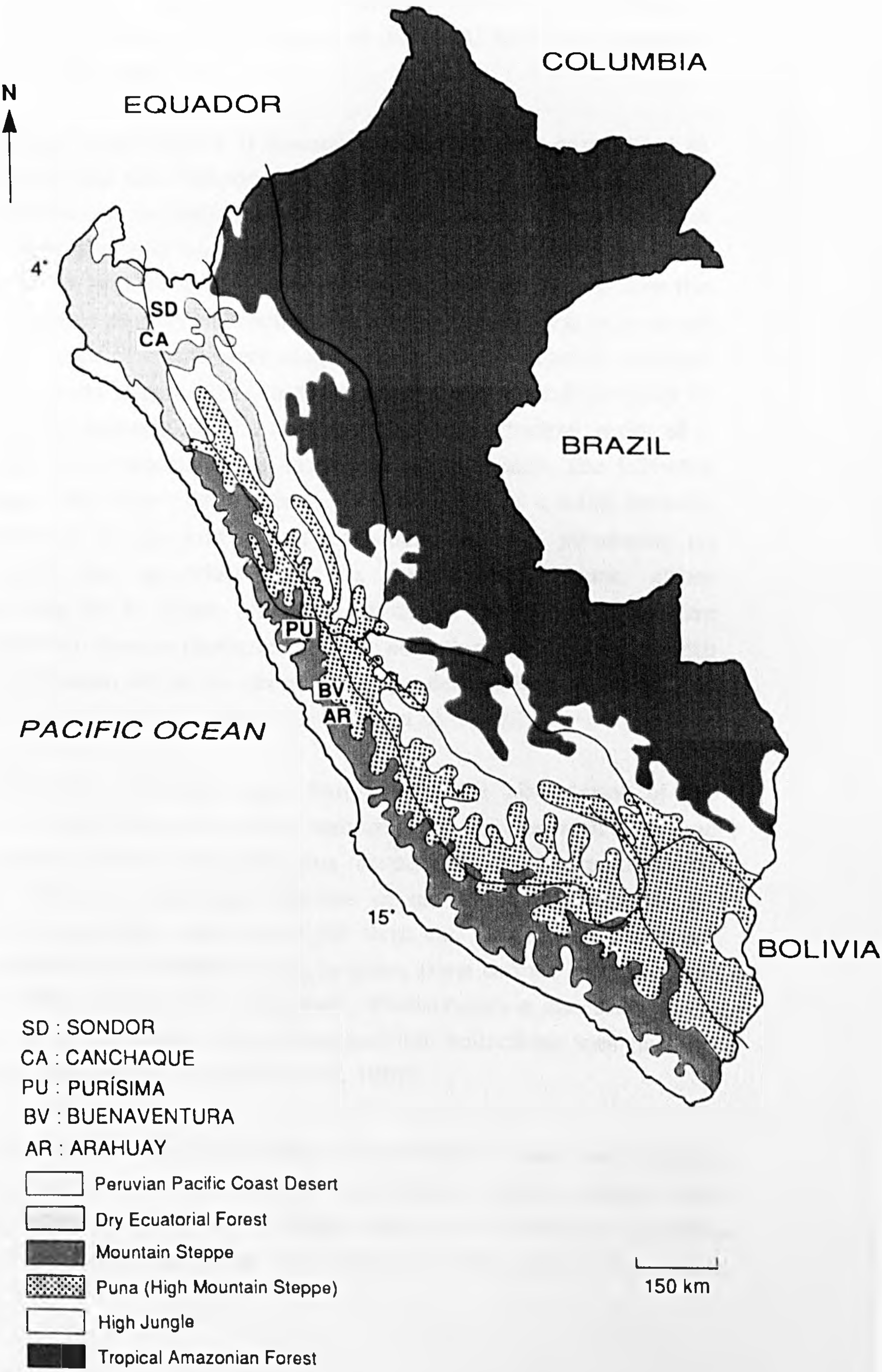
Gilardi *et al.* (1988) in Israel reported the association of local environmental factors with CL rate in non-immune soldiers. They found 15-fold greater morbidity in subjects living on a wadi than on a higher ridge during the high infectivity periods (March to August). The two sites were just 350 meters apart. The authors emphasized the importance of microenvironmental factors, but did not assess which local factors were involved.

B. Review of transmission patterns of Andean cutaneous leishmaniasis in Peru.

In Peru four *Leishmania* species have been described: *L. braziliensis*, *L. peruviana*, *L. guyanensis*, and *L. mexicana* (Arana *et al.* 1990, Llanos-Cuentas & Davies 1992). Only the first two have epidemiological importance. The disease named uta (Andean cutaneous leishmaniasis due to *L. peruviana*) produces cutaneous lesions and, sporadically, mucosal involvement by both contiguity and metastasis (Llanos-Cuentas 1991). Uta is distributed between 4°S to 15°S in inter-Andean valleys 800-3,000 meters above sea level (asl) of the West, Central and Eastern Andes, though the main transmission occurs in the Pacific-facing Andes (Figure 1). A rough estimation using the distribution of the disease by Departments suggest that *L. peruviana* causes approximately 30% of the cases reported in the country. The cumulative prevalence of uta (scars + lesions) varies between 14 and 92% depending on the town (Herrer 1957, LLanos-Cuentas unpublished data).

Prior to our own current studies, evidence for the vector status of various phlebotominae sandflies, and the place of transmission, was largely circumstantial (Villaseca *et al.* in press). At least 12 *Lutzomyia* (*Lu.*) species (Diptera: *Psychodidae*: *Phlebotominae*) have been identified in sandfly collections made in endemic areas of uta (E. Perez, personal communication). A major difficulty has been to separate the vectorial roles of the sympatric anthropophilic species *Lu. peruensis* and *Lu. verrucarrum* (Llanos-Cuentas & Davies 1992). *Lu. ayacuchensis* is a third potentially

FIGURE 1. LOCATION OF FIVE UTA ENDEMIC REGIONS IN PERU.



important anthropophilic species. It is the likely vector of uta in endemic valleys in Ayacucho Department (Cáceres *et al.* 1991) and the suspected vector in Piura department.

In Purisima region (Figure 1) quantitative studies were carried out in order to relate spatial and temporal variation in sandfly abundance with concurrent variation in the incidence of uta (Villaseca *et al.* in press). The incidence and prevalence of uta were measured in a cohort study of 1,778 inhabitants from 36 hamlets and villages for two years (1987-1989). Over the same period monthly sandfly collections (indoors and outdoors) were made at two fixed stations. Attempts were also made to detect naturally infected sandflies. The results suggest that in the Purisima valley, and probably in ecologically similar endemic areas, *Lu. peruensis* is the principal vector of *L. peruviana*, and that transmission is mainly intradomiciliary. The following findings support this view : (i) a significant correlation ($p < 0.05$) between monthly incidence of uta and indoor abundance of *Lu. peruensis*; no correlation with the abundance of *Lu. peruensis* outdoors, either peridomestic only or in crops (Villaseca *et al.* in press), (ii) a positive association between disease incidence and the abundance of this vector with the altitude (Villaseca *et al.* in press), (iii) the demonstration of natural infection of *L. peruviana* in *Lu. peruensis* (Perez *et al.* 1991).

Althought no correlation was found with the abundance of *Lu. verrucarrum* in this valley, laboratory transmission studies with colonized flies and golden hamsters (*Mesocricetus auratus*) have shown that this species can transmit *L.peruviana* (Davies *et al.* in press). Because *Lu. verrucarrum* is frequently more abundant than *Lu. peruensis* in endemic areas, its potential role in transmission in some areas cannot be discounted (Perez *et al.* 1992, Davies *et al.* in press). Furthermore a specimen of *Lu. verrucarrum* caught outdoors from anthropophilic collections was naturaly infected with a *Leishmania* spp (Perez *et al.* 1992).

A study to determine the relative importance of man and domestic animals as blood sources for sandflies was done in Chaute, Rimac valley, Department of Lima (Perez *et al.* 1992). Monthly collections of sandflies indoors and outdoors were made over one year (1990-1991). The results suggest: (i) in total, the main sources of blood for sandflies in the vicinity of houses are domestic animals rather than humans for both *Lu. peruensis* (54% indoors and 79% outdoors) and *Lu. verrucarrum* (69% indoors and 71% outdoors); (ii) by species, humans are probably the most important sources of blood (meals mainly indoors); (iii) 11 species of domestic animals were sources of blood; cows, cats, dogs and goats were most frequently detected.

In addition, a further analysis of data published by Perez *et al.* (1992) showed that indoors *Lu. peruensis* was less endophilic than *Lu. verrucarrum*; 293 (8.4%) of 3,470 sandflies collected indoors were identified as *Lu. peruensis* and 3,177 (91.6%) were *Lu. verrucarrum* ($p < 0.001$). Outdoors 31.6% (988/3,131) were *Lu. peruensis* and 68.3% (2,140/3,131) were *Lu. verrucarrum*. But *Lu. peruensis* was more anthropophilic among bloodfed *Lu. verrucarrum*. Sandflies caught indoors 42.3% of *Lu. peruensis* had human blood vs 31.2% of *Lu. verrucarrum* ($p=0.04$). There was no difference in human blood index of these species outdoors (man-biting catch). These results strengthen the role of *Lu. peruensis* as the principal vector of uta (Villaseca *et al.* in press).

Additional observations in Purisima valley and other endemic areas indicate the possibility of extra-domiciliary rural transmission. For instance, persons who lived in villages located over 3,000 meters asl where there are no sandflies must have acquired the disease when working at lower altitude in their crops. Recently, the evaluation of incidence in susceptible children and adults in different endemic areas of uta (16 towns) showed strong differences by age between towns of the same valleys, and also between valleys (Llanos-Cuentas & Davies 1992). In some areas children are largely affected, whilst in other areas the disease occurs mainly in adults. This finding reinforces the idea that there are different patterns of transmission even for villages in the same valley. In some places transmission occurs mainly around dwellings, whilst in others transmission is mostly extradomiciliary. A combination is of course possible too.

Circumstantial evidence for transmission outside the domestic arena comes from a recent analysis of the effect of DDT on uta. Between the 1950s and 1970s, DDT was used as a residual insecticide in houses as part of antimalarial campaign in Peru. Davies *et al.* (submitted) made a retrospective analysis of the annual incidence rate in the uninfected population from 1901 to 1993 in two endemic valleys of uta in the Department of Lima and found strong evidence that DDT temporarily suppressed the transmission of uta in some towns, but in others no reduction in incidence was observed. The latter were towns located over 3,000 meters asl.

Wild and domestic reservoirs were studied in Purisima valley between 1987 and 1989 (Llanos-Cuentas & Davies 1992) in monthly captures. The fauna were restricted, 3 genera and 8 species were captured. From 471 wild animals tested for *Leishmania* infection, flagellates were observed in 56. Of these, only three strains were identified as *Leishmania* (all *L. peruviana*): one from the opossum *Didelphis albiventris* and two from the rodent *Phyllotis andinum*. 643 dogs were examined for lesions compatible with leishmaniasis using the criteria described by Herrer & Battistini (1951). All were negative except one dog; and sequential parasitological (smears and *in vitro* cultures) examinations of this dog were negative too. 90 serum sample from dogs were collected and evaluated by Dot-ELISA; 23% of samples were positive to dilution of 1/200 (Guevara & Paredes 1992), though no evaluation for cross-reactivity was made. Recently, *Leishmania* parasites have been isolated from three dogs of Purisima valley and two from Canta valley. New studies are ongoing in order to determine (i) the rate of infection of dogs and wild animals using the polymerase chain reaction and/or classical parasitological methods, and (ii) the potential role of dogs by transmission experiments.

In summary, our review of the literature on uta transmission supports the following: (i) *Lu. peruensis* is probably the principal vector of *L. peruviana*, *Lu. ayacuchensis* is the likely vector in some endemic areas (i.e. Ayacucho Department) and *Lu. verrucarrum* is a potential vector in some areas, (ii) there is indirect evidence for transmission inside houses, such as the association between incidence (annual or monthly) of uta and indoor abundance of *Lu. peruensis* and the temporary suppression of uta transmission after DDT spraying in houses, and (iii) there is indirect evidence of extradomiciliary transmission in persons who lived in villages over 3,000 meters asl.

C. Approach and Objectives of the Present Study

C.1. The Approach

There are still important gaps in our knowledge of the transmission of uta, despite recent advances: we do not know what proportion of cases arise by transmission inside houses, around houses or away from houses, we have a poor idea of the risk factors associated with all three modes of transmission, and we have little idea how much disease could be reduced by control programs. This information is crucial to resolve important questions such as how we can avoid resurgence of uta after it has been suppressed by spraying insecticide in dwellings, and what alternative approaches to control might be less expensive, and more practical and efficacious in the long term.

There are two basic approaches to investigating causality: one works from cause to effect and the other works from effect to cause (Schelesslman 1982, pp. 7-24). We are using two approaches to study the sites of transmission of uta: (i) investigating the risk factors associated with transmission using a case-control design (this thesis) , and (ii) manipulating the domiciliary (inside and outside) sandfly populations, by house fumigation to identify whether any reduction in incidence ensues.

Case-control design is a relatively new methodology for evaluating risk factors in common diseases such as leishmaniasis (Smith 1982, Rodrigues & Kirkwood 1990).Case-control methodology was initially developed as an alternative to experimentation, because experiments are often ethically or logistically impossible. A major strength of the case-control design compared with other types of epidemiological research is that it permits simultaneous evaluation of many causal hypotheses. It can also be applied directly to human beings (Breslow & Day 1980). A major weakness is the susceptibility to bias, specially selection bias, resulting in non comparable information from cases and controls. However, the new designs can, in part, avoid these problems, e.g. with a good definition of study base, cases and controls, and by using short periods of person-time in order to diminish recall bias.

The assumption that case-control works only in rare diseases changed after Miettinen (1976) argued that incident cases and controls could be recruited concurrently rather than 'after the end of the entire risk period of interest'. Miettinen (1976) also showed how to calculate relative rate using this design. The approach has been more fully developed in recent years (Greenland & Thomas 1982, Smith *et al.* 1984, Prentice 1986, Rodrigues & Kirkwood 1990) jointly with new developments in statistical methodology (Breslow & Day 1980, Hosmer & Lemenshow 1989, Wacholder 1991), and with new computer software for analysis (e.g. Epidemiological Graphics, Estimation, and Testing package [EGRET], SAS System programs). Together these provide a new research tool for epidemiological studies.

Here we describe a population-based case-control study with a concurrent design comparing persons who developed Andean cutaneous leishmaniasis (uta) against persons who did not. Cases and controls were matched by age, sex and place of residence. The unit of analysis was person-time. The main exposure groups were: characteristics of the house, environmental characteristics around the house, and behaviour patterns of people.

C.2. The Objectives

1. To identify characteristics of houses that are associated with the risk of infection.
2. To identify environmental factors around houses that are associated with the risk of infection.
3. To identify human behaviour patterns that are associated with risk of infection.

CHAPTER II: MATERIAL AND METHODS

The following sections present the study area, study design and methodos of analysis.

A. Study Area

The study area consisted of 25 villages and hamlets located in five areas, endemic for Andean cutaneous leishmaniasis, located in the West Andean highlands of Peru (Figures 1 to 5). The Working Group on Leishmaniasis (WGL) at Universidad Peruana Cayetano Heredia (UPCH), Instituto de Medicina Tropical 'Alexander von Humboldt' (IMTAvH) has been conducting epidemiological research in these endemic areas for the last seven years. The majority of these communities have signed letters of consent, agreeing to broad cooperation with the WGL. WGL has provided free diagnosis and treatment to all cases of leishmaniasis.

The ecological and climatic characteristics of Arahuay, Buenaventura and Purisima are very similar (Table 1, Figures 1 to 3, 6a & 6b). Arahuay and Buenaventura belong to two adjacent valleys in the same Department (Figure 2). High mountains with steep slopes and low temperatures are characteristic of these valleys. The flora and fauna are not abundant, and are restricted to deep parts of the valleys. Canchaque and Sondor are located in Piura Department (Figures 4, 5, 7a & 7b). The former is at the source of the Piura river; it has the characteristics of high jungle, but no primary vegetation (Peñaherrera 1990). Sondor is located close to the Huancabamba river in a transition zone between high jungle and paramo (Brack 1987). These regions are flatter, with more abundant flora and fauna than mountain steppe regions (Brack 1987). Temperatures are higher in Canchaque than in Sondor area. However, each valley represents a spectrum of micro-ecological conditions depending the latitude, altitude, water supply and human intervention. The rainy season in all regions under study is usually from December to April, and the dry season is from April to

Figure 2. Location of Study Villages in Arahuay and Buenaventura Regions, Province of Canta, Department of Lima, Perú.

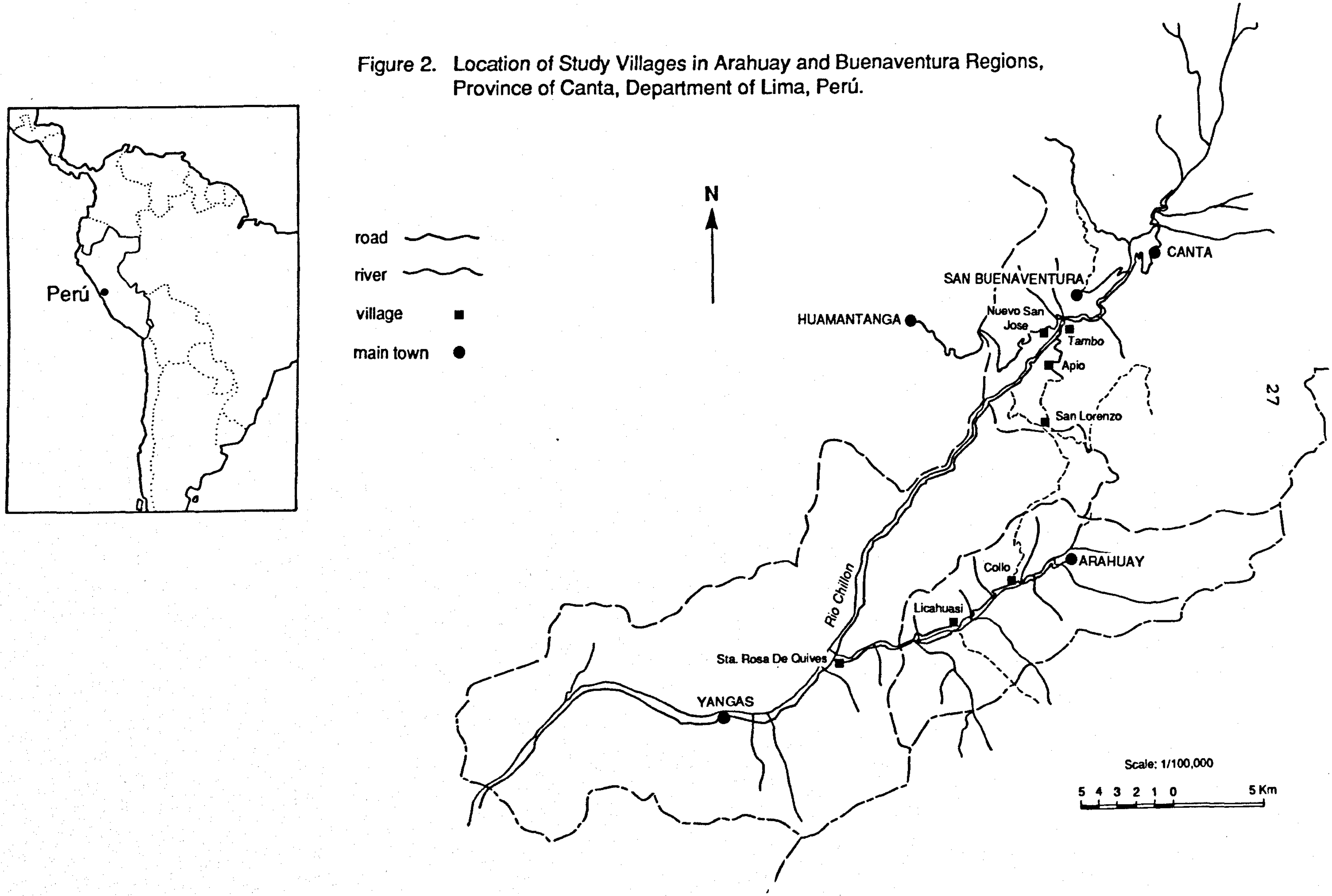


Figure 3. Location of Study Villages in Purísima Region, Province of Bolognesi, Department of Ancash, Perú.

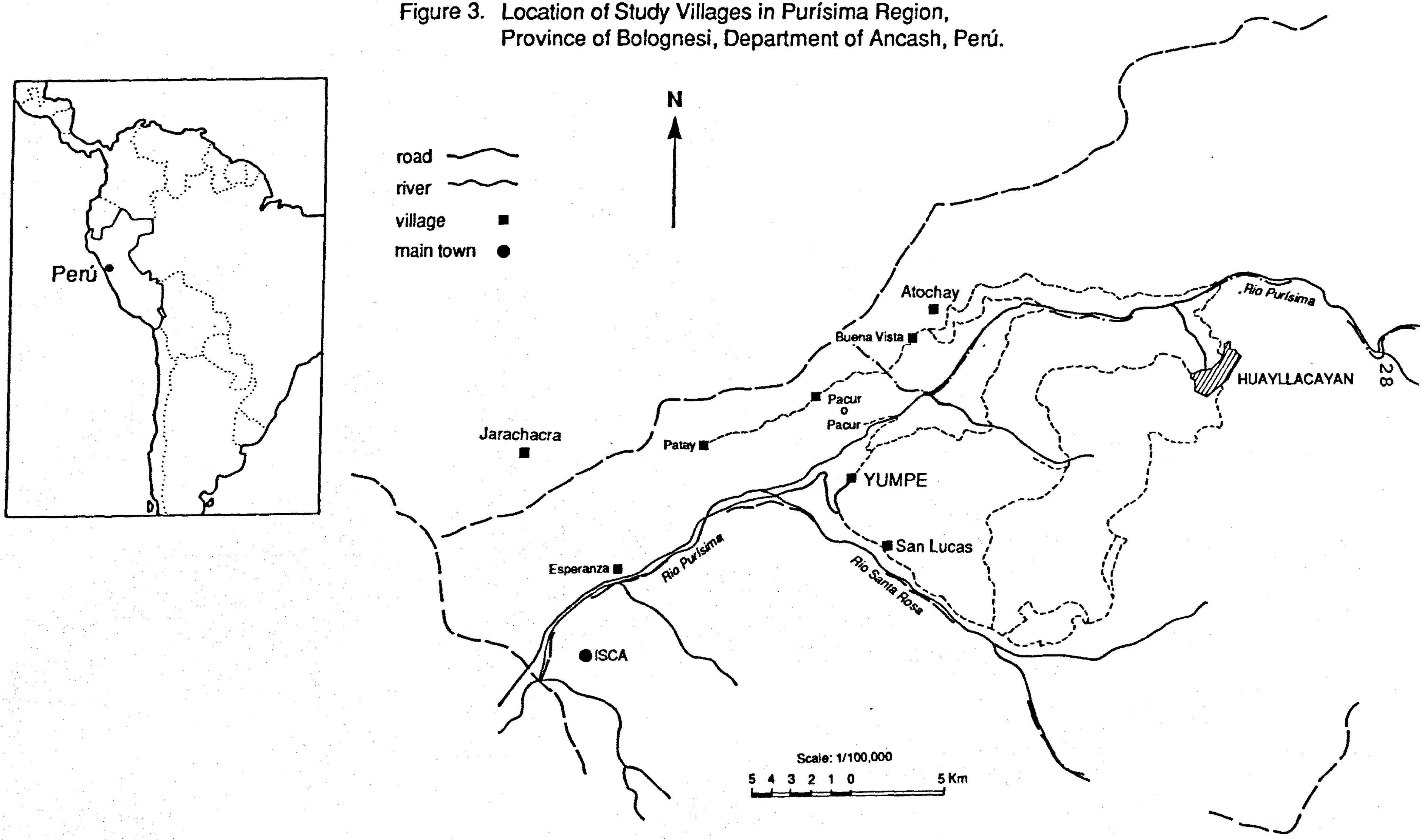


Figure 4. Location of Study Villages in Canchaque Region, Province of Huancabamba, Department of Piura, Perú.

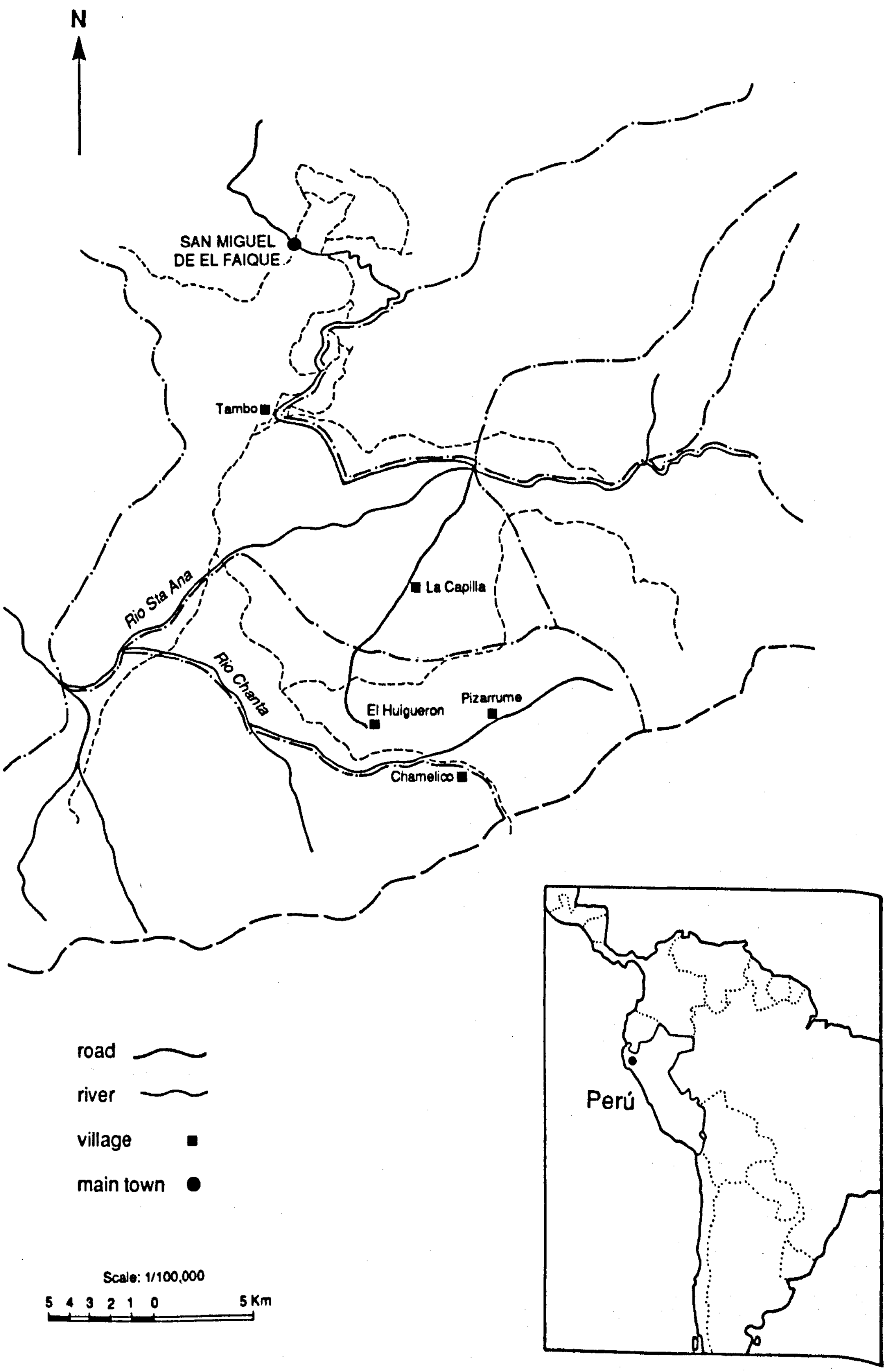


Figure 5. Location of Study Villages in Sondor Region, Province of Huancabamba, Department of Piura, Perú.

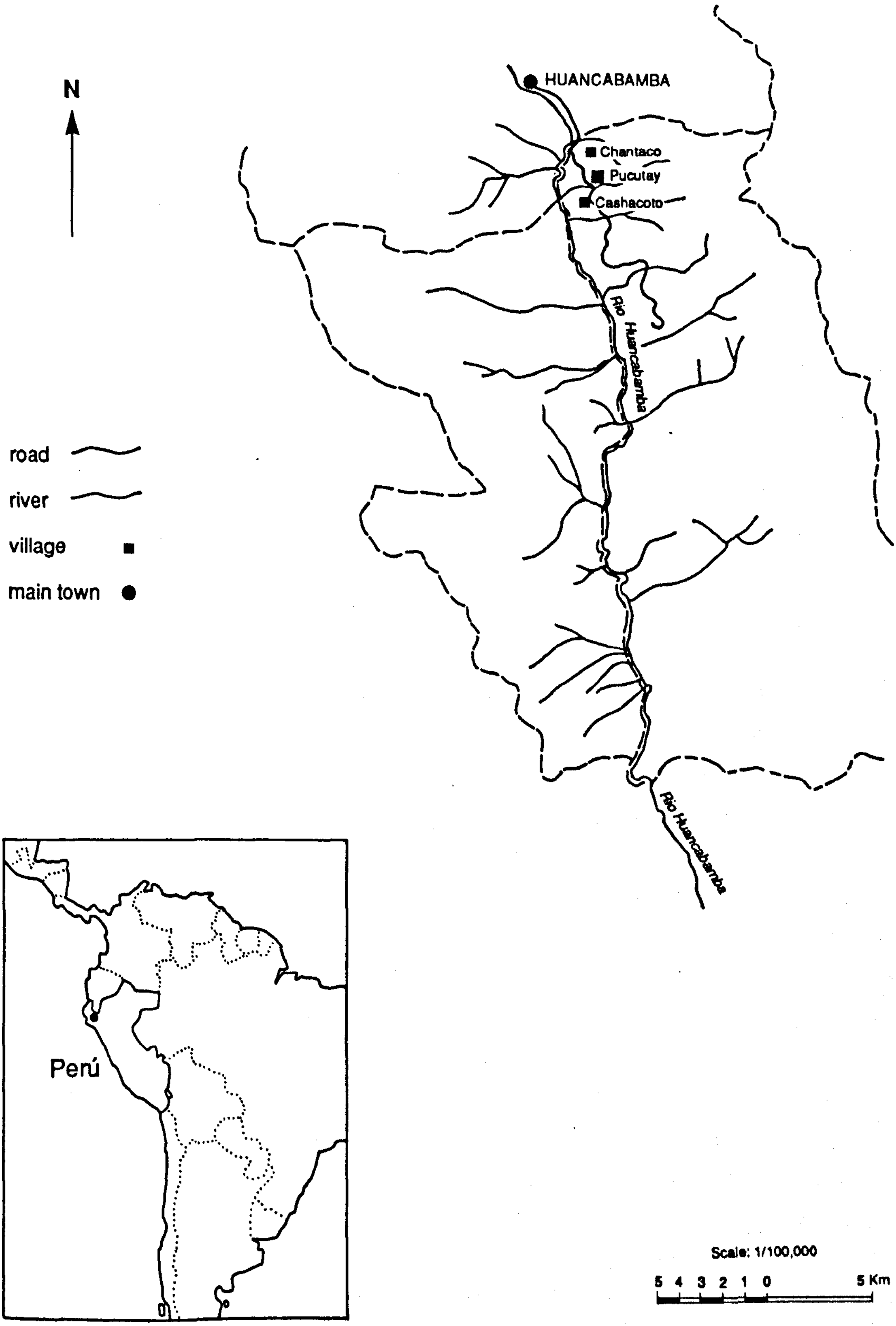


Table A.O.1. Ecological and Climatological Characteristics in the Study Area.

Regions	Ecoregion	Altitude (masl)	Geology	Climate	Temperature (mean ^{o}C)
Arahuay	Mountain Steppe	2000-3000	Lower Cretaceoun	Boreal Cold	13.1-15
Buenaventura	Mountain Steppe	2000-3000	Upper Cretaceo	Boreal Cold	13.1-15
Purísima	Mountain Steppe	1900-3100	Lower Cretaceo	Boreal Cold	13.0-15
Canchaque	High Jungle	1000-2000	Lower Cretaceo	Temperate Moderate Rainy	21.1-23
Sondor	Paramo	1900-2300	Tertiary Quaternary	Temperate	13.1-17

Ref: Brack, A. (1987).

Figure 6a. Ecological Characteristics of Buenaventura area, Region 1

Figure 6b. Ecological Characteristics of Purísima area, Region 1

Figure 7a. Ecological Characteristics of Sondor area, Region 2

Figure 7b. Ecological Characteristics of Canchaque area, Region 2

November. The sites in Ancash and Lima Departments we group together and name region 1, and the sites in Piura Department, region 2.

Houses are frequently located near to sources of water (waterways, springs, etc.). Villages and hamlets are usually connected by unpaved roads and horse paths. The houses within the permanent settlements are constructed primarily of regional materials; the walls are usually of adobe, bricks or sometimes stone, with a corrugated iron or thatched roof. In region 2 the houses are bigger, usually with two floors, and not constructed of stone.

The main activity is subsistence farming, supplemented with a few cattle, goats or sheep. Families usually own small plots (the mean in region 1 is approximately 1 acre and in region 2 more than 2 acres) located in different parts of a valley, at different altitudes. Most fields are bordered by dry stone walls (pircas). Walking times from field to village varied between 10 minutes and three hours.

The valleys in region 1 are unforested and most of the area around the villages is irrigated for the cultivation of fruit trees (e.g. apples, peaches, avocado), cereals (e.g. maize, wheat), root vegetables (e.g. potato, sweet potato, yuca) and legumes (e.g beans, alfalfa). In region 2, in Canchaque area, the more common crops are coffee, cereals (maize), fruit trees (e.g. oranges, lemons, bananas), legumes (pumpkins, beans, peas), root vegetables (yuca), sugar cane and forage; in Sondor area cereals (e.g. maize, bean, wheat), and tubers (e.g. potato, yuca). A variety of demestic animals are kept, sometimes in walled corrals, and include sheep, goats, chickens and guinea pigs in region 1 and pigs, goats, cows and cats in region 2. Frequently, households own more than one dog. For each valley (both regions) there is usually one river, with temporary tributaries which carry water for less than six months of the year. The crops are seasonal and they vary according to water availability, but families usually work simultaneously on several plots and crops. This complex, subsistence microagriculture demands the participation of all family members, including children. Frequently, adult men take charge of the land preparation, sowing and transporting produce; the women work more on harvesting, weeding and irrigation, and the children (over 5 years old) help by shepherding or by looking after the harvest. Women normally take children (from a few months after birth) to their places of work.

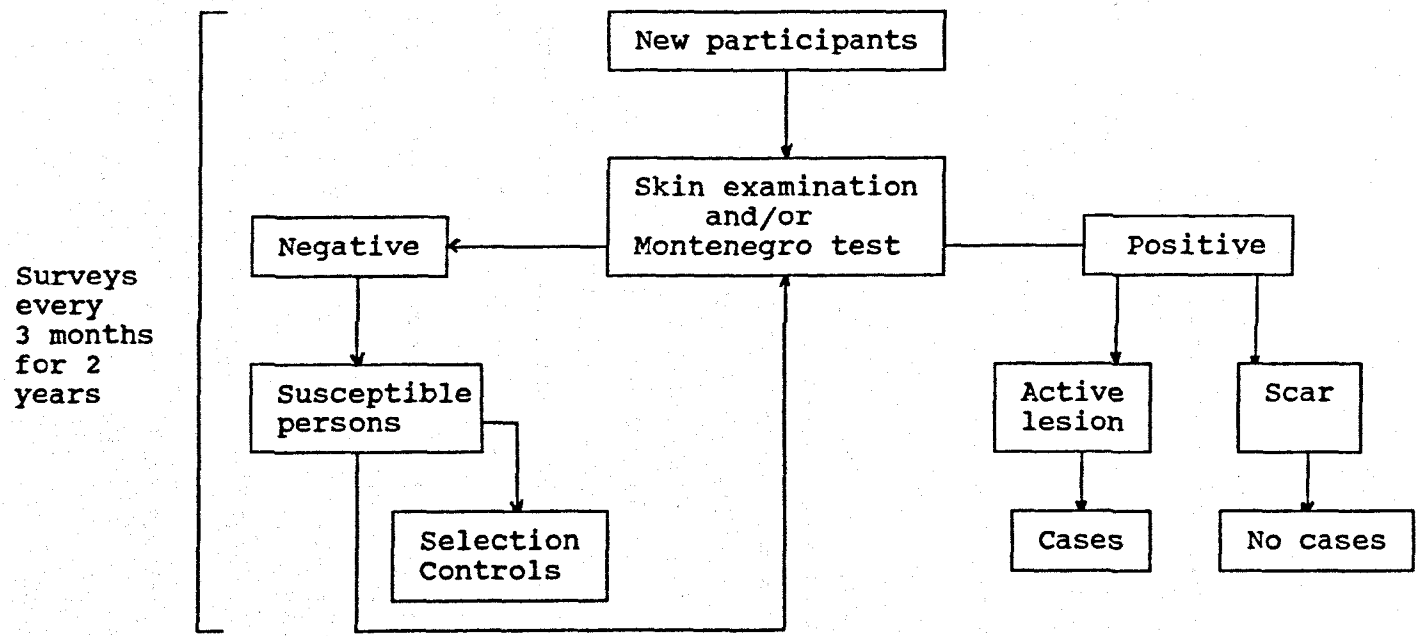
Children usually start to go to a local school at age 6 and most leave at age 15. Migration towards the large coastal cities is high in adolescents. There are no large land owners in these valleys and the socioeconomic conditions are more or less similar for the majority of families.

B. Study Design

On the first visit, a large scale map of each community in each region was prepared, locating the site of each homestead. The census was carried out between January and July, 1991. All houses in every area were identified with a village and household number. All residents of each community were registered. Date of interview, identification (sequentially assigned numbers), altitude, date of birth, sex, relation to head of household of all permanent residents, and complete family history of CL and the results of Montenegro skin-test (positive, negative or not done) were recorded. Persons were questioned about their current disease status, and examined for the characteristic scars and/or lesions associated with CL. All persons with cutaneous lesions were carefully examined in the first instance by highly trained workers (more than 3-5 years experience each at the time of start the study), and later usually by a specialist in tropical diseases.

In this concurrent design, the controls were selected from those still at risk when a new case was diagnosed. A person originally selected as a control could, during the course of study, become a case (Rodrigues & Kirkwood 1990). Figure 8, summarizes the framework of the study. The population base of this case-control study was defined as the set of persons-time that lived in Arahuay, Buenaventura, Purisima, Canchaque and Sondor areas for a period of at least 6 months (a semester) between October 1990 to December 1992 (study period), in which susceptible subjects became cases (Schlesselman 1982, p.15; Wacholder *et al.* 1992a). Person-time was defined as the length of time each person stayed at risk during the study period,

Figure 8. FRAMEWORK DESIGN



starting in October 1990. The unit of person-time used was the person-semester.

Cases were those persons who belong to the base and who developed their first leishmanial cutaneous lesion at any time during the study period. A corresponding control was selected from those still susceptible. Controls were persons who where (i) skin-test negative and skin-examination negative for leishmanial lesions [scars or active] at the start of the study, and (ii) skin-examination negative at the time a case was identified. Persons who acquired the disease were no longer at risk, and therefore no longer eligible for selection as controls.

Cases and controls were matched by age, sex, and village of residence. The age requirements differed for children and adults. For cases under 15 years, all potential controls aged within 2 years of the case were included. For cases > 15 years, controls were selected from among those persons closest in age to the case, but within a maximum range of +/- 10 years. The objective of these criteria was to obtain a minimum of one control and a maximum of three controls per case. The criteria for exclusion of both cases and controls was to have been away from the home village for more than 2 weeks in the six months prior to enrollment.

Each homestead was revisited every three months from March 1991 to December 1992. At each visit, all suspected cases occurring since the last visit were recorded (Figure 8). When patients consented, confirmation of disease status was undertaken by parasitological diagnosis. Patients were included in a open clinical trial comparing the efficacy of Glucantime administrated by parenteral or intralesional injection, following to the schedule suggested by WHO (1990). At the same time, primary health care and education was provided for the whole community.

B.1. Selection of cases and controls and surveillance

Cases (CL patients) were identified by a combination of two approaches: (i) Active detection of new cases by field workers, who visited all houses in the 25 hamlets or villages selected for this study every three months through the two years of surveillance. The majority of cases were discovered this way. (ii) Passive detection by nurses and/or health personnel over the same period of time at several Health Posts: El Higueron in Canchaque valley; Arahuay, Collo, San Jose in Canta valley; and Yumpe in Purisima valley.

Because there is a wide diversity of morphological characteristics in lesions of CL, all non-typical lesions were evaluated by the author (who has more than 10 years' experience with leishmaniasis). Controls were found immediately after the suspected case was defined. The records for each family (by community) were always available to the interviewer. All candidate controls were examined again by a second member of the team in order to detect any suspected leishmanial scars. Risk factors were recorded every time that any person was selected either as a case or a control.

B.2. Diagnosis

A possitive clinical diagnosis of active leishmaniasis-like lesions was recorded when any person developed one or more skin lesions with the following characteristics: (1) located on exposed areas of the body, (2) usually painless lesions (pain is normally due to bacterial superinfection), frequently infiltrative, or infiltrative with a central shallow ulcer (3) satellite nodular lesions in and/or around the borders, (4) ulcerating lesions with deep granulomatous tissue and raised borders with induration, (5) localized adenopathy (present in early stages of the disease), and (6) no self-cure over 4 weeks.

The diagnosis of uta fell into three categories of certainty: (1) suspected: clinical diagnosis only, (2) probable: clinical diagnosis of uta plus positive Montenegro skin test [see below]; and (3) definitive: clinical diagnosis plus parasitological demonstration of *Leishmania sp* [see below]. For the purpose of this study, cases were taken from groups (2) and (3).

Patients were examined for evidence of other chronic systemic diseases, and for evidence of mucosal disease (anterior rhinoscopy and examination of the mouth and throat). All patients with the latter condition were excluded because mucosal involvement is not a primary lesion, and their disease would have started before the study period. Characteristically, leishmanial scars have a depressed surface in the center, covered by thin hyperpigmented skin and rounded contours (meaning no sharp angles) with fine concentric ring-like traces.

Montenegro skin-test and serology using DotELISA was carried out for all suspected cases and controls. The antigen for skin testing was prepared from a reference strain of *L. peruviana* (MHOM/PE85/LP053) at IMTAvH. The suspension had 30 μg/ml of protein nitrogen and 0.1 ml of the antigen was inoculated intradermally in the right forearm. Mean induration equal to or more than 5 millimeters at either 48 or 72 hours was taken as positive. Procedures for inoculation and for the reading of skin-tests were standardized between field workers. Antigen was kept at -20^{o} C.

Parasitological diagnosis was by microscopy on skin smears, and/or by *in vitro* culture from isolates following the procedures described by Cuba *et al.* (1984). Parasitological evaluations were always offered in suspected or atypical lesions. These evaluations were performed for consenting adults or, in the case of children, with the consent of the parents. Biopsies were performed on cutaneous lesions using a 2mm punch (the small size chosen to minimize discomfort because lesions were frequently located on the face) after local anesthetic (Lidocaine 1%) and before the start of treatment. Imprint smears were prepared for direct examination, fixed in methyl alcohol, stained with Giemsa and searched for parasites at IMTAvH. The biopsy material was incubated for three or four hours in saline solution with the following antibiotics: 180 ug/ml penicillin, 300 ug/ml streptomycin and 150 ug/ml 5-fluorocytosine (Romero *et al.* 1987). It was then homogenized in a tissue grinder, and the crude supernatant was put into Difco blood agar (biphasic medium with 15% rabbit blood).

Patients with non-characteristic lesions, or those with an inadequate therapeutic response (follow-up every 3 months), were further evaluated for other possible aetiologies. Samples were cultured to isolate fungi (Sabouraud's medium) and/or mycobacterias (Zeil Neilsen medium) and/or studied histopathologically. The biochemical identification of the strains isolated was carried out by isoenzyme procedures described by Arana *et al.* (1990).

B.3. Data collection

Specific questionnaires were prepared for recording potential risk factors for the transmission of uta (Appendix 1). Particular effort was made to define highly objective and closed-ended questions or variables which could be easily measured. Whenever possible, the same information was obtained in more than one way. The questionnaires were tested in a pilot study in a community outside the study area. Additional forms were used to record epidemiological and clinical data (Appendices 2 and 3).

The collected data were personal histories, characteristics of the interiors and exteriors of houses, and behaviours. Dates of birth, specially in older persons, were sometimes deduced with the help of relatives. Migrations up to a year before the interview date were carefully determined, but only the information for the previous six months (the period of interest) was used for the analysis. As most inhabitants have more than one occupation, all were recorded.

All potentially relevant features within 300 meters (m) of the house were measured by the interviewer. Distances greater than 300 m were entered as 400 m for the purposes of the analysis.

Repair or replacement of walls, roofs, floors, and pircas, or built walls contiguous with pre-existing walls and insecticide sprayed inside the house up to 12 months before the date of interview were examined for risk of transmission.

The time spent on farming activities was only recorded up to three months before the date of interview in order to reduce recall bias. Subjects usually worked more than one plot on the same day, and all were recorded.

The time of appearance of a cutaneous lesion was easily determined: surveillance every 3 months permitted us to detect early lesions, and enquires were made to determine the month they began. If the subject could not provide a consistent date, other members of the family helped us to determine the time of onset using dates of local or national events (i.e. football results, relatives birth dates, community activities, etc). The following additional clinical information was recorded: number, type, location and size (graph separately in the vinyl sheet scars and active lesions) of the lesions; and information about prior therapy (Appendix 3).

All field workers were trained in order to standardize the methodology for diagnosis (scars or active lesions). Questionnaires with risk factors were completed by one person only. The supervisor checked the information but was not permitted to change data. Inadequate or apparently incorrect information was re-checked in the field. The communities and the interviewers were unaware of the aims of this study. The information about risk factors (both cases and controls) was usually obtained before confirming the diagnosis of each case. When the cases and controls were children, relevant information was obtained from a guardian or parent.

B.4. Sample Size

A preliminary estimate of sample size suggested that between 161 and 190 cases would be required, with their respective controls. This number included an allowance of 25% for possible losses or nonresponse, and was calculated from the following factors (Cousens *et al.* 1988): (i) the magnitude of association, R, in which we were interested in detecting an odds ratio equal to, or over 2; (ii) the proportion of the population exposed to the risk factors of interest, P, which was between 30% to 70%; (iii) 5% of level of significance, S, and (iv) 80% power, T. The relevant formulae are (Cousens *et al.* 1988):

$$N = [\,2\,C\,(1 - C)\,(S+T)^2\,] \,/\, (P-A)^2$$

Where $A = PR \,/\, [\,1 + P\,(R+1)\,]$ and $C = (A + P)\,/2$

C. ANALYSIS

C.1. Data Processing

A coding scheme was devised for all variables of interest. The magnetic data format was standard XBase (DBF/DBT), which is readable by any dBASE-compatible program Software for data entry and checking was developed using FoxPro V4.0 running under IBM DOS 4.2. The data were coded from the forms into the program without intermediate transcription.

C.2. Data analysis

Factors were divided in four groups, according to common characteristics. Thus, group I assessed the characteristics of the house, group II characteristics around the house, group III human indoor behaviour and group IV human outdoor behaviour. A stratified analysis by region and age group was carried out because these were the more likely source of interactions.

A screening of probable associations between both discrete or continuous factors was made using descriptive statistics (frequencies, histograms, medians, modes, means, plot, etc). Because of the low frequency of some categorical variables by strata they were divided into exposed and unexposed categories. After an inspection of the simple tabulations and the screening results, some variables were re-coded. Some aggregate variables were created for behavioural activities, where an outcome was the result of more than one measure variable. One such outcome was 'days in plots in last 3 months' (the total number of days that every case or control spent in plot(s) during the last 3 months). Frequently families had more than one plot. Then it was necessary to add the days expended in each plot. All variables of Table A.IV.2 were calculated by the same means.

For matched analyses, factors were recorded as dichotomous variables, their association tested using a bivariate statistical test (Manzel-Haenzel method with Yates' correction when necessary) and matched odds ratios (MOR) calculated. The continuous variables were also stratified into two strata in order to calculate their MORs. The cut-off point for each variable was subjectively chosen by a combination of the median and/or mean and/or the proportional distribution of samples among groups, ensuring sufficient sample sizes within groups.

The approach to choosing the best model for multivariate analysis was to use any variable which, after careful matched analysis for association (pooled or by region), had p-value < 0.25 (Bendel & Afifi 1977, Mickey & Greenland 1989). Dummy variables were generated for discrete factors. Multivariate analysis was done in EGRET using conditional logistic regression, with a multiplicative model. Cases were coded as "1" and controls as "0".

Models for the whole study area (pooled data) were constructed and then for regions 1 & 2 separately. Factors were added group by group. The model was then extended adding the interactions by region for all factors in previous model. Finally, we incorporated interactions by age group. For each of the above models, additional models were built to include or exclude different factors. The best model was chosen by comparison of the log of the ratio of the maximized likelihoods. To compare the fit of two models we compared the log of the ratio of the maximized likelihood for the first to the maximized likelihood for the second.

Population attributable risk (PAR) was calculated with the formula proposed by Bruzzi *et al.* (1985) for a multiplicative setting, using data from pair-matched case-control. The relevant formula is:

$$PAR = 1 - \sum_j (p_j / R_j)$$

Where PAR = population attributable risk, p_j = proportion of cases in the jth exposure stratum, R_j = risk ratio in the jth exposure stratum.

Case-control study provides the distribution of exposures among the population using the distribution of factors among cases only, and the estimates of relative risk (Bruzzi et al. 1985). The latter was estimated from ORs calculated by concurrent design (Bruzzi et al. 1985). Regression coefficients calculated by multivariate analyses were adjusted for other variables included in the model and represent the log odds ratios.

The data were transferred from FoxPro into Epi-Info, version 5.01 (EPI5) as well as SPSS/PC+ V4.0 for descriptive analysis. The matched analyses were done in EPI5, the multivariate analyses in EGRET version 0.26.6, and PAR calculated with a program written by Dr Miguel Campos at UPCH (see Appendix 6). The output from SPSS was incorporated into Microsoft Word 5.0 files, together with text. Tables and graphs were prepared in Quattro Pro V4.0 and Software Publishing Harvard Graphics 2.13.

CHAPTER III. RESULTS

STUDY POPULATION

In total 4,454 persons participated in this study, distributed in 5 regions: Arahuay, Buenaventura, Purisima, Canchaque and Sondor (Figure 1, Table 2).

During the study period 572 individuals (206 as cases and 366 as controls) were admitted and 522 (91.3%) of them (187 cases and 335 controls) achieved the inclusion criteria. Nineteen of 206 (9.2%) persons admitted as cases were excluded: five (2.4%) were both skin-test and parasitologically negative, eight (3.9%) were parasitologically negative and had incomplete skin-test data, and six (2.9%) had no controls.

Thirty-one controls (8.5%) were excluded: 29 because their cases failed to satisfy the inclusion criteria, and two because they refused the skin-test.

Table 3 summarizes the diagnostic results. Definitive diagnosis was achieved on 40% of occasions (75/187). Thirty-two patients (18.6%) mainly children did not consent to parasitological procedures. The Montenegro skin-test was applied in all cases, although it could not be read in 12. All these individuals were parasitologically positive. Parasites were isolated from two patients (2/173, 1.2%) who were MST negative. Of 75 isolates from cutaneous lesions 64 were identified as *L.peruviana*. Of 11 isolates not identified, 10 did not adapt well to *in vitro* culture conditions and one was contaminated with fungus.

In the five regions selected for this study, we found neither Chagas' disease, nor its vectors. Viseral leishmaniasis has not been described in Peru.

Because of the high prevalence of disease (scars plus active lesions) in many villages and hamlets in this study (between 50% to 90%), the number

Table A.O.2. Altitude, Population, Number of Cases and Controls by Village and Extension by Region in Study Area.

Village/Hamlet	Altitude (m asl)*	Total Number of persons	Number of Cases	Number of Controls
Arahuay Region				
Arahuay	1500	375	8	13
Collo	2000	171	9	12
Licahuasi	1700	186	3	7
Subtotal		732	20	32
Buenaventura Region				
San B.Ventura	2600	149	4	7
San Lorenzo	3000	125	2	3
Apioviscas	2650	202	14	20
San Jose Nuevo	2350	119	9	11
Tambo	2000	47	2	3
Subtotal		642	31	44
Purísima Region				
Iscas	1700	50	5	5
La Esperanza	1850	111	4	12
San Lucas	2250	60	5	6
Buena Vista	2650	146	5	12
Yumpe	2200	144	10	21
Jarachacra	2540	105	2	2
Pucur&Macpara	2650	75	3	3
Patay	2600	41	3	8
Actochay	2700	37	2	2
Subtotal		769	39	71
Canchaque Region				
Tambo	1200	89	4	9
El Higueron	1450	384	36	70
La Capilla	1450	502	23	48
Pizarrumi	1750	186	7	10
Chamelico	1500	230	14	25
Subtotal		1391	84	162
Sondor Region				
Cashacoto	2000	502	6	10
Chantaco	2000	375	6	14
Pucutay	2000	132	1	2
Subtotal		1009	13	26
Total		4543	187	335

* m asl: meters above sea level

Table A.O.3. Diagnosed Cases of Andean Cutaneous Leishmaniasis

Result	Skin Test		Parasitological Exams[1]		Total[2]	
	N	(%)	N	(%)	N	(%)
Positive	173	(92.5)	75	(40.1)	187	(100)
Negative	2	(1.1)	80	(42.8)	0	
Not done	12	(6.4)	32	(17.1)	0	
Total	187	(100.0)	187	(100.0)	187	(100)

1: combination of smear plus in vitro culture

2: Montenegro skin test and/or parasitological exams of controls per case varied: 45 (24.1%) cases had 1 control, 136 (72.7%) cases had 2 controls and 6 (3.2%) cases had 3 controls. The overall ratio of controls to cases was 1.8.

During the study period 11 controls became cases. All but one developed the disease after the period of interest (after the six months that they were used as controls).In seven matched pairs, the case and at least one of the controls were in the same house.

A. DESCRIPTIVE ANALYSIS (MAIN TABULATIONS)

Tables A.0.1 to A.IV.2 present the main study findings as bivariate comparisons between cases and controls. 187 cases and 335 controls were entered into the tabulation procedure. These tables are intended to display frequency distributions and to provide a first idea of associations from unadjusted comparisons. Since the main conclusions will be drawn from the matched and multivariate analyses, no statistical tests were performed at this stage.

Table A.0.1 presents general variables of the study. All persons were mixed between Indian/Caucasian "mestizos" and the majority were catholic (98%). Uta is primarily a disease of children. The first episode affected 84% children (43% were less than 5 years old) and only 16% adults. The youngest patient was 2 months of age and the oldest 61 years. Both sexes were affected by the disease in similar proportions. Both, cases and controls showed similar distributions for age, sex and place of infection. The numbers of cases and controls found in Lima plus Ancash Departments were roughly equal to those in Piura Department. Cases were usually (81%) located and admitted to the study within 4 months of the onset of disease.

The distribution of cases and controls was similar by birth Department, region of residence and occupation (Table A.0.2). The majority were born in the same area as they were infected. Place of infection is further detailed in Figures 2 to 5. Principal occupations were farming and shepherding. A large number of persons were simply accompanying working

Table A.0.4. General Variables
Case-Control Study on Cutaneous Leishmaniasis, Peru 1990-1992

Variables	Total		Group			
			Cases		Controls	
	n	%	n	%	n	%
Age group (years) *						
Less than 1	39	7.47	17	9.18	22	6.57
1 - 4	184	35.24	63	33.68	121	36.12
5 - 14	224	42.91	77	41.17	147	43.88
15 - 39	59	11.30	24	12.97	35	10.45
40 +	16	3.06	6	3.20	10	2.98
Total	522	100.00	187	100.00	335	100.00
Sex *						
Male	239	45.78	89	47.60	150	44.78
Female	283	54.22	98	52.40	185	55.22
Total	522	100.00	187	100.00	335	100.00
Place of infection *						
Lima	127	24.33	51	27.27	76	22.69
Ancash	110	21.07	39	20.86	71	21.19
Piura	285	54.61	97	51.87	188	56.12
Total	522	100.00	187	100.00	335	100.00
Montenegro skin test						
Positive	173	33.14	173	92.51	0	0.00
Negative	337	64.56	2	1.07	335	100.00
Not read	12	2.30	12	6.42	0	0.00
Total	522	100.00	187	100.00	335	100.00
Race						
Mixed	522	100.00	187	100.00	335	100.00
Religion						
Catholic	511	97.89	331	98.81	180	96.26
Protestant	11	2.11	4	1.19	7	3.74
Total	522	100.00	187	100.00	335	100.00

* Variables used to match

Table A.0.5 Variables of Birth Department, Region of Residence and Occupation
Case-Control Study on Cutaneous Leishmaniasis, Peru 1989-1991

Variables	Total		Group			
			Cases		Controls	
	n	%	n	%	n	%
Birth Department						
Ancash	103	19.73	38	20.32	65	19.41
Cajamarca	1	.19	1	.53	0	.00
Cerro de Pasco	1	.19	0	.00	1	.29
Lima	134	25.67	52	27.81	82	24.47
Piura	278	53.26	96	51.34	182	54.33
San Martin	5	.96	0	.00	5	1.50
Total	522	100.00	187	100.00	335	100.00
Regions of residence						
Arahuay	52	9.96	20	10.69	32	9.56
Buenaventura	75	14.37	31	16.58	44	13.13
Purísima	110	21.07	39	20.86	71	21.19
Canchaque	246	47.13	84	44.91	162	48.36
Sondor	39	7.47	13	6.96	26	7.76
Total	522	100.00	187	100.00	335	100.00
Occupations *						
Farmer	135	25.86	54	28.88	81	24.18
School Child	195	37.36	72	38.50	123	36.72
Shepherd	85	16.28	31	16.58	54	16.12
Labourer	1	0.19	1	.53	0	0.00
Companion	217	41.57	73	39.04	144	42.99
Teacher	1	0.19	0	0.00	1	0.30
Housewife	29	5.56	10	5.35	19	5.67
Other	52	9.96	17	9.09	35	10.45

* Some persons had more than one occupation

adults, because they were under 5 years old, though some children in this age group helped their parents look after the crops. Only a small number of women (5%) list 'housewife' as their sole occupation.

Table A.1.1 shows the materials used to build houses; Table A.I.2 presents the house characteristics treated as discrete variables; and Table A.I.3 additional continuous variables. The questions concerning the house intended to discriminate between houses built with regional and rural material (potentially with higher risk) and houses built with modern materials (i.e. bricks, cement, corrugated iron). Covering of the floors, walls and roof addressed the availability of sandfly resting places inside the house. Common characteristics of houses were walls built with unfired mud bricks (adobe, 98%), usually un-faced (69%), with a corrugated iron (calamine) roof (79%) without a ceiling or floor covering (73%) and uncovered floor (73%). Cases were twice as frequent as controls in stone houses. Cases were also more frequent in houses with unfinished walls. Controls were more frequent in houses having cement floors (Table A.I.1). Some houses were built from a combination of different regional materials. Roof material had no apparent effect on the distribution of cases and controls.

Houses throughout the study area frequently had only one or two floors (99%), between 2 to 4 rooms (67%) and 1 to 2 bedrooms (79%) (Table A.I.2). Kitchens were generally inside houses (77%) in a common room used also for dining and sleeping. In 81% of indoor kitchens, a crude chimney served as a smoke exit, and these were more common in cases than in controls. Only very few people (2%) did not use firewood to cook (Table A.I.2).

38% of houses had a latrine, and only a small fraction of these were appropriately used (Table A.I.2). Similar distances to, and numbers of, latrines were observed in cases and controls (Table A.I.3).

The numbers of windows in houses and bedrooms, the presence of open areas and covers over windows explored the degree to which sandflies could enter houses, and/or evaluated the role of lighting during the day. Information on whether windows were usually open or closed was supplied

Table A.I.1. House Characteristics: Floor, Wall and Roof Materials
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

	Total*		Group			
	n	%	Cases*		Controls*	
			n	%	n	%
Floor cover						
Uncover	383	73.27	145	77.54	238	71.05
Cement	121	23.28	36	19.25	85	25.37
Wood	18	3.45	6	3.21	12	3.58
Wall material						
Stone	43	8.24	24	12.83	19	5.67
Adobe	407	77.97	140	74.87	267	79.70
Bricks	10	1.91	2	1.07	8	2.39
Miscellaneous	62	11.88	21	11.23	41	12.24
Roof material						
Tile	16	3.76	5	2.67	11	3.28
Calamine	414	79.42	146	78.07	268	80.00
Thatched	90	17.34	35	18.72	55	16.42
Missing	2	0.38	1	0.54	1	0.30
Wall cover						
Un-faced	362	69.34	138	73.80	224	66.90
Clay	101	19.34	29	15.51	72	21.46
Cement	6	1.15	1	0.54	5	1.50
Plaster	34	6.51	13	6.94	21	6.27
Miscellaneous	19	3.66	6	3.21	13	3.87

* number of cases: 187, number of controls: 335, total: 522

Table A.I.2. House Characteristics: Discrete Variables
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

	Total*		Group			
	n	%	Cases*		Controls*	
			n	%	n	%
Floor number						
1	210	40.23	66	35.29	144	42.99
2	306	58.62	121	64.71	185	55.22
3	6	1.15	0	.00	6	1.79
Rooms number						
1	24	4.60	8	4.28	16	4.78
2	100	19.16	41	21.93	59	17.61
3	144	27.59	49	26.20	95	28.36
4	83	15.90	32	17.11	51	15.22
5+	171	32.75	57	30.48	114	34.03
Bedroom number						
1	258	49.43	100	53.48	158	47.16
2	154	29.50	55	29.41	99	29.55
3+	110	21.07	32	17.11	78	23.29
Number of windows in house						
0	91	17.43	30	16.04	61	18.21
1 - 2	225	43.10	83	44.39	142	42.39
3 - 6	188	36.02	66	35.31	122	36.42
7 - 12	18	3.45	8	4.26	10	2.98
Daytime house lighting						
Dark	477	91.38	175	93.58	302	90.15
Half Light	45	8.62	12	6.42	33	9.85
Daytime bedrooms lighting						
Dark	402	77.01	149	79.68	253	75.52
Half Light	120	22.99	38	20.32	82	24.48
Kitchen location						
Inside	402	77.01	139	74.33	263	78.51
Outside	120	22.99	48	25.67	72	21.49
Chimney						
Yes	422	80.84	163	87.17	259	77.31
No	100	19.16	24	12.83	76	22.69
Latrine						
Yes	196	37.55	71	37.97	125	37.31
No	326	62.45	116	62.03	210	62.69

* number of cases: 187, number of controls: 335, total: 522

Table A.I.3 House Characteristics: Continuous Variables
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Variables	Number	Mean	Std.Dev	Min	Max
Residence time (months)					
Cases	187	72.82	82.41	1.00	660.00
Controls	335	72.21	68.25	1.00	540.00
Total	522	72.43	73.56	1.00	660.00
Age of the house (months)					
Cases	187	222.05	210.71	9.00	1188.00
Controls	335	256.16	225.67	3.00	1188.00
Total	522	243.94	220.83	3.00	1188.00
Bedroom size (sq.m)					
Cases	187	26.99	71.76	1.50	980.00
Controls	335	37.09	129.38	3.15	1600.00
Total	522	33.47	112.22	1.50	1600.00
House window open					
Cases	187	0.99	1.38	0.00	7.00
Controls	335	0.91	1.42	0.00	9.00
Total	522	0.94	1.40	0.00	9.00
Holes in house windows less bedrooms (sq.cm)					
Cases	187	8.77	54.95	0.00	684.00
Controls	335	4.29	22.66	0.00	254.00
Total	522	5.90	37.50	0.00	684.00
Holes in bedroom windows (sq.cm)					
Cases	187	7.88	30.25	0.00	246.00
Controls	335	4.43	23.25	0.00	246.00
Total	522	5.67	26.42	0.00	246.00
Kitchen distance (m)					
Cases	187	1.43	3.78	0.00	100.00
Controls	335	1.10	5.80	0.00	100.00
Total	522	1.21	5.16	0.00	100.00
Latrine distance (m)					
Cases	187	131.19	88.48	1.00	200.00
Controls	335	131.20	89.57	3.00	200.00
Total	522	131.20	89.10	1.00	200.00

Std.Dev: Standard Deviation, Min: Minimum, Max: Maximum
sq.m: Square meters, sq.cm: Square centimeters

by the occupants, while holes in windows of bedrooms or others rooms of the house were variables measured by the interviewer.

The mean of number of windows was 2.5 (range 0 to 12), usually kept closed during the day. Less than 1.5% of windows had glass. The most frequent window coverings were wooden or plastic sheets and cardboard, all usually with holes or cracks. Holes in windows of both bedrooms and others rooms were more common in cases than controls (Table A.I.3) but their frequency was low, particularly in region 1. Although the confidence intervals were wide, the data suggested that controls tended to live in older houses, with bigger bedrooms than cases (Table A.I.3). We comment below on the role of lighting during the day.

Distance from house to hill, creek, road, waterway, river, pirca, and/or neighbouring kitchen garden was measured to examine associations between ecological or geographic characteristics surrounding the house (possible sandfly resting or breeding sites) and risk of uta (Table A.II.1). Houses of cases were more commonly situated on or near creeks, close to waterways, and by a neighbour with a kitchen gardens themselves. Houses of controls were located more commonly near a river, close to a road, and more frequently had kitchen gardens. The location of houses with respect to hills and dry stone walls ("pircas") was not different between cases and controls. Only four persons had temporary refuges near their houses.

Possible associations between some species of plants surrounding houses and transmission were investigated. Groups of trees around houses were rare. The majority of wild plants were xerophytes found together with cultivated plants such as root vegetables, legumes and fruit trees. Peridomiciliary plants are further detailed on Table A.II.2. 1535 plant specimens were recorded and classified into 23 families; 20% of the specimens could not be identified because the regional names do not appear in the floras used. The distribution of families of plants was not different in cases and controls.

Tables A.III.1 to A.III.4 present the characteristics of houses modified by human activities and reported by the study subjects. The data show that

Table A.II.1 Features Around the House
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Variables	Number	Mean	Std.Dev	Min	Max
Distance to hill (m)					
Cases	187	118.67	156.72	1.00	400.00
Controls	335	127.17	159.78	1.00	400.00
Total	522	124.12	158.59	1.00	400.00
Distance to creek (m)					
Cases	187	283.27	160.14	1.00	400.00
Controls	335	303.90	152.14	1.50	400.00
Total	522	296.51	155.21	1.00	400.00
Distance to road (m)					
Cases	187	100.09	139.16	0.50	400.00
Controls	335	81.67	134.24	0.50	400.00
Total	522	88.27	88.27	0.50	400.00
Distance to river (m)					
Cases	187	343.04	126.29	1.50	400.00
Controls	335	315.05	152.75	1.50	400.00
Total	522	325.08	144.33	1.50	400.00
Distance to waterways (m)					
Cases	187	109.15	89.07	0.20	200.00
Controls	335	122.25	89.11	0.50	200.00
Total	522	117.56	89.23	0.20	200.00
Distance to kitchen garden (m)					
Cases	187	330.48	296.13	1.00	600.00
Controls	335	275.68	294.48	1.00	600.00
Total	522	295.96	295.31	1.00	600.00
Distance to neighbouring kitchen garden (m)					
Cases	187	14.77	17.74	1.00	80.00
Controls	335	10.30	9.60	1.00	80.00
Total	522	12.10	13.60	1.00	80.00
Distance to stone walls (pircas) (m)					
Cases	187	4.56	4.66	1.00	80.00
Controls	335	5.81	8.66	1.00	80.00
Total	522	5.34	7.44	1.00	80.00
Extension of pircas (m)					
Cases	187	49.75	71.09	1.00	566.00
Controls	335	45.69	77.26	1.00	566.65
Total	522	47.20	74.90	1.00	566.65

Table A.II.2 Peridomiciliary Features: Plants
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Value Label	Value	Frequency	Percent	Valid Percent	Cum Percent
Not coded		321	20.9	20.9	20.9
Anonaceae	ANO	75	4.9	4.9	25.8
Apiaceae	API	7	.5	.5	26.3
Apocinaceae	APO	5	.3	.3	26.6
Betulaceae	BET	2	.1	.1	26.7
Bixaceae	BIX	13	.8	.8	27.6
Cactaceae	CAC	5	.3	.3	27.9
Caricaceae	CAR	25	1.6	1.6	29.5
Convulvulaceae	CON	12	.8	.8	30.3
Euphorbiaceae	EUP	19	1.2	1.2	31.5
Fabaceae	FAB	107	7.0	7.0	38.5
Gramineae	GRA	187	12.2	12.2	50.7
Lauraceae	LAU	152	9.9	9.9	60.6
Mimosaceae	MIM	41	2.7	2.7	63.3
Myrtaceae	MIR	1	.1	.1	63.3
Musaceae	MUS	102	6.6	6.6	70.0
Passifloraceae	PAS	57	3.7	3.7	73.7
Rosaceae	ROS	195	12.7	12.7	86.4
Rubiaceae	RUB	36	2.3	2.3	88.7
Rutaceae	RUT	121	7.9	7.9	96.6
Salanaceae	SAL	52	3.4	3.4	100.0
	Total	1535	100.0	100.0	

cases had modified their houses (the previous year) more recently than controls. Notice that, in each strata of modification, the number of houses was small (Table A.III.1). Sometimes more than one modification occurred at the same time. New houses were recorded as a modification when built using the walls of a neighbour's house.

The distribution of cases and controls by insecticide use in houses was similar. Usually the spraying was deficient (inadequate equipment, low concentration, incorrect spraying sites), with insufficient coverage.

The importance of intensity of light during the day and at night are summarized in Tables A.I.1 and A.III.2. It should be noted that the daytime house lighting (Table A.I.1) was observed by the interviewer, and that frequently, the visit occurred early in the morning or late in the afternoon. Cases and controls show a similar distribution for daytime house lighting intensity. Because there is no electricity in the rural areas of our study, people used a variety of lamps at night. They were usually used between 18.00 hours (sunset) and 20.30 hours (bed time). The intensity of the light varied with the type of lamp. The "Petromax" produced higher illumination (from gaseous kerosene), but was not frequently used because of its high cost. Home-made kerosene and proprietary kerosene lamps were more generally used and illumination from the former is better (smoke darkens the glass of the later). Controls tended to use proprietary lamps more frequently (Table A.III.1).

Length of occupation in the house, number of permanent and temporary residents and number and species of domestic animals were recorded to explore their importance in attracting the vector inside or around the dwellings.

Cases and controls were similarly distributed by number of residents and length of residence in the house (Tables A.III.2). No differences were observed when residents were stratified as permanent or temporary. Only the permanent residents were used for subsequent analysis.

Table A.III.1 Human Indoor Behaviour: Discrete Variables
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Variables	Total		Group			
			Case		Control	
	n	%	n	%	n	%
House Modification (< 1 year)						
Yes	83	15.90	38	20.32	45	13.43
No	439	84.10	149	79.68	290	86.57
Type of Modification						
More rooms	14	2.68	7	3.74	7	2.09
Larger rooms	6	1.15	2	1.07	4	1.19
New walls	19	3.64	9	4.81	10	2.99
New house	13	2.52	5	2.73	8	2.40
Repair/replacement:						
wall covers	6	1.16	2	1.09	4	1.20
roofs	15	2.91	8	4.37	7	2.10
floors	1	0.19	0	0.00	1	0.30
kitchen	10	1.94	3	1.64	7	2.10
doors/windows	6	1.16	3	1.64	3	0.90
walls	1	0.19	0	0.00	1	0.30
others	7	1.36	4	2.19	3	0.90
Sprayed insecticide (< 1 year)						
Yes	73	13.98	24	12.8	49	14.63
No	449	86.02	163	87.1	286	85.38
Kerosene Lamp:						
.Petromax						
Yes	7	1.34	5	2.67	2	0.60
No	515	98.66	182	97.33	333	99.40
.Home-made						
Yes	269	51.53	99	52.94	170	50.75
No	253	48.47	88	47.06	165	49.25
.Proprietary						
Yes	297	57.12	97	52.94	200	59.88
No	223	42.88	89	47.85	134	40.12
Candles						
Yes	27	5.17	9	4.81	18	5.37
No	495	94.83	178	95.19	317	94.63
Kitchen type						
Firewood	512	98.08	185	98.93	327	97.61
Kerosene	9	1.72	2	1.07	7	2.09
Firewood+kerosene	1	0.19	0	0.00	1	0.30

Table A.III.2 Human Indoor Behaviour: Continuous Variables
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Variable	Number	Mean	Std.Dev	Min	Max
Length of occupation the house					
Cases	187	3.95	1.57	1.00	6.00
Controls	335	4.17	1.52	1.00	6.00
Total	522	4.09	1.54	1.00	6.00
Number of residents					
Cases	187	7.12	2.24	2.00	14.00
Controls	335	7.18	2.66	2.00	16.00
Total	522	7.16	2.51	2.00	16.00
Number of permanent residents					
Cases	187	6.19	2.07	0.00	13.00
Controls	335	6.25	2.33	1.00	14.00
Total	522	6.23	2.24	0.00	13.00
Number of temporary residents					
Cases	187	0.89	1.21	0.00	8.00
Controls	335	0.93	1.55	0.00	7.00
Total	522	0.92	1.43	0.00	8.00

Table A.III.3. Human Indoor Behaviour: Stored Products in House
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

	Total		Group			
			Case		Control	
	n	%	n	%	n	%
Stored products in house						
Yes	464	88.89	167	89.30	297	88.66
No	58	11.11	20	10.70	38	11.34
Where stored:						
Common room	191	36.59	62	33.16	129	38.51
Bedroom	127	24.33	53	28.34	74	22.09
Living room	98	18.77	37	19.79	61	18.21
Basement	20	3.83	6	3.21	14	4.18
Kitchen	13	2.49	5	2.67	8	2.39
Nixed	73	.19	24	.53	49	.00
Seeds						
No	157	30.08	60	32.09	97	28.96
Chickpeas	127	24.33	36	19.25	91	27.16
Beans	159	30.46	58	31.02	101	30.15
Lentils	69	13.22	30	16.04	39	11.64
Grains						
No	81	15.52	33	17.65	48	14.33
Maize	253	48.47	77	41.18	176	52.54
Wheat	152	29.12	66	35.29	86	25.67
Barley	36	6.90	11	5.88	25	7.46
Root vegetables						
No	341	65.33	122	65.24	219	65.37
Potato	152	29.12	58	31.02	94	28.06
Yucca	11	2.11	5	2.67	6	1.79
Sweet Potato	17	3.26	2	1.07	15	4.48
Fruits						
No	488	93.49	170	90.91	318	94.93
Apple	20	3.83	7	3.74	13	3.88
Abocado	8	1.53	5	2.67	3	.90
Wood						
No	494	94.64	171	91.44	323	96.42
Yes	28	5.36	16	8.56	12	3.68
Green vegetables						
No	480	91.95	171	91.44	309	92.24
Yes	42	8.05	16	8.56	26	7.76

Table A.III.4. Human Indoor Behaviour: Domestic Animals
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Variable	Number	Mean	Std.Dev	Min	Max
Guinea pigs					
Cases	187	2.37	3.78	0.00	20.00
Controls	335	2.99	4.57	0.00	30.00
Total	522	2.77	4.31	0.00	30.00
Cows					
Cases	187	0.53	2.15	0.00	20.00
Controls	335	0.22	1.11	0.00	12.00
Total	522	0.33	1.57	0.00	20.00
Horses					
Cases	187	0.33	0.69	0.00	5.00
Controls	335	0.40	0.91	0.00	9.00
Total	522	0.37	0.84	0.00	9.00
Goats					
Cases	187	0.74	2.12	0.00	14.00
Controls	335	0.86	2.51	0.00	14.00
Total	522	0.82	2.37	0.00	14.00
Sheep					
Cases	187	0.69	1.84	0.00	17.00
Controls	335	0.52	1.51	0.00	14.00
Total	522	0.58	1.64	0.00	17.00
Pigs					
Cases	187	0.87	1.54	0.00	13.00
Controls	335	0.99	1.66	0.00	13.00
Total	522	0.94	1.62	0.00	13.00
Chickens					
Cases	187	4.63	5.54	0.00	25.00
Controls	335	5.81	7.41	0.00	50.00
Total	522	5.39	6.81	0.00	50.00
Cats					
Cases	187	0.19	0.47	0.00	2.00
Controls	335	0.24	0.52	0.00	3.00
Total	522	0.23	0.51	0.00	3.00
Dogs					
Cases	187	0.87	1.06	0.00	6.00
Controls	335	1.00	1.16	0.00	6.00
Total	522	0.95	1.13	0.00	6.00

The recording of data on stored agriculture products (i.e. seeds, grains, fruits, root vegetables, etc) or wood inside houses was intended to evaluate roughly associations between natural reservoirs (temporal migration near the dwellings) and risk of transmission.

Table A.III.3 presents the findings for household stored products. Both cases and controls kept stored products in comparable proportions. Products were stored in all rooms of the house, including bedrooms. Because there are often no walls between rooms, or rooms only partially divided, there is no justification to stratify by room type in following analysis. The data suggested a different distribution in cases and controls with some products such as beans, broad beans, maize, wheat (Table A.III.3). The majority of these products were seasonal, particularly fruits, roots and green vegetables.

Table A.III.4 presents the distribution of domestic animals in dwellings. Of 1,942 animals recorded, 328 (17%) slept in the house, 1555 (80%) up to 30 meters from the house and 59 (3%) beyond this distance. Of 22 species recorded, 13 were rare. Cats (72%) and guinea pigs (73%) commonly slept inside the house; only 7/340 (2%) of the dogs did so. The distribution of all species of domestic animals except cows was similar in cases and controls. In general, the number of animals per family was low, the mean by species was low with high a standard deviation (Table A.III.4). The mean number of dogs per householder was about 1, but 43% (224/522) of the study population did not have a dog at the time of interview.

Possible associations between behaviour of inhabitants of the endemic areas outside the house, such as repairing of waterways, roads, pircas, cutting of wood, or irrigation work at night, and increased risk of disease were explored.

Families in endemic areas usually had more than 1 field (65%) and in 89% of instances they were situated outside the village. The mean was 2.3 fields per person and only 9% had more than 5 fields. 18.4% of persons did not own fields. Of 1394 fields, 201 (22%) bordered creeks, 1056 (76%) on hillsides and 33 (2%) elsewhere. Only 92 (13.8%) of fields had constant

Table A.IV.1 Human Outdoor Behaviour: Continuous Variables
Case-Control Study on Cutaneous Leishmaniasis, Peru 1989-1991

Variables	Number	Mean	Std.Dev	Min	Max
Repairing waterways					
Cases	187	0.20	0.74	0.00	5.00
Controls	335	0.09	0.36	0.00	2.00
Total	522	0.13	0.51	0.00	5.00
Repairing roads					
Cases	187	0.59	0.12	0.00	3.00
Controls	335	0.14	2.76	0.00	30.00
Total	522	0.11	1.35	0.00	30.00
Repairing or building pircas					
Cases	187	0.09	0.48	0.00	5.00
Controls	335	0.25	1.91	0.00	30.00
Total	522	0.19	1.56	0.00	30.00
Weeding					
Cases	187	15.05	26.55	0.00	180.00
Controls	335	18.35	39.62	0.00	180.00
Total	522	17.17	35.50	0.00	180.00
Cutting wood					
Cases	187	2.20	14.01	0.00	180.00
Controls	335	1.21	10.27	0.00	180.00
Total	522	1.57	11.75	0.00	180.00
Irrigation work at night					
Cases	187	0.60	2.39	0.00	24.00
Controls	335	0.87	7.76	0.00	98.00
Total	522	0.77	6.37	0.00	98.00

Table A.IV.2. Human Outdoor Behaviour: Crops
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Variables	Number	Mean	Std.Dev	Min	Max
Number of plots					
Cases	187	2.36	1.71	0.00	7.00
Controls	335	2.21	1.83	0.00	8.00
Total	522	2.26	1.79	0.00	8.00
Days in plots (< 3 months)					
Cases	187	33.94	35.21	0.00	90.00
Controls	335	31.52	32.49	0.00	90.00
Total	522	32.39	23.00	0.00	90.00
Times slept at plot (< 3 months)					
Cases	187	0.40	0.68	0.00	3.00
Controls	335	0.32	0.79	0.00	8.00
Total	522	0.34	0.76	0.00	8.00
Number of plots on creeks					
Cases	187	0.58	0.93	0.00	5.00
Controls	335	0.43	0.76	0.00	4.00
Total	522	0.48	0.83	0.00	5.00
Days in creeks (< 3 months)					
Cases	187	6.35	15.93	0.00	90.00
Controls	335	5.15	16.21	0.00	90.00
Total	522	5.58	16.11	0.00	90.00
Number of plots on slopes					
Cases	187	1.63	1.46	0.00	6.00
Controls	335	1.66	1.59	0.00	7.00
Total	522	1.65	1.55	0.00	7.00
Days on slopes (< 3 months)					
Cases	187	25.73	32.27	0.00	90.00
Controls	335	24.28	28.78	0.00	90.00
Total	522	24.80	30.05	0.00	90.00
Number of plots elsewhere					
Cases	187	0.11	0.49	0.00	3.00
Controls	335	0.09	0.38	0.00	3.00
Total	522	0.10	0.42	0.00	3.00
Days in elsewhere (< 3 months)					
Cases	187	1.51	9.28	0.00	90.00
Controls	335	1.83	10.32	0.00	90.00
Total	522	1.71	9.95	0.00	90.00

irrigation. The number and location of fields were comparable in controls and cases.

Tables A.IV.1 and A.IV.2 present human outdoor activities that could be related to transmission of the disease. Fishing and hunting are rare in uta areas and were not included in these tables. Repairing waterways, roads and pircas showed strong differences of their means between cases and controls (Table A.IV.1), but only the former is reliable. The standard deviation of controls in repairing roads and pircas was very high in comparison with their cases. A larger proportion of cases than controls was involved in repairing waterways during the day. Cutting wood was twice as frequent among cases than controls. A common attribute of variables of Table A.IV.1 was their low frequency in the study population. Farming activities and behaviour of cases and controls with respect to crops were similar, except occasions slept at plots (Table A.IV.2). People had more plots on slopes than in creeks, and were at the former 5 times longer. Sleeping in fields was not a common behaviour.

All variables analyzed through descriptive statistics except those with very low frequency were included in matched analysis.

B. MATCHED ANALYSIS

In order to maintain the same sequence of analysis as used in section A of this chapter, the candidate variables for risk factors of transmission were analyzed in the same four groups: characteristics of the house, geographic or physical features around the dwelling, and human behavior indoors and outdoors.

Because the ecological characteristics of region 1 (Lima plus Ancash Departments) are different from those in region 2 (Piura Department), and because CL is a disease mainly of children, the analysis was stratified by region and age group. The latter stratification was made between persons less than 15 years (named children) and 15 years or more (named adults) on the basis of working patterns.

Tables B.I.1 to B.IV.2 summarize the whole study findings evaluated by matched pairs, Tables C.I.1 to C.IV.2 the results of matched analyses stratified by region, and in Tables D.I.1 to D.IV.1 by age group.

Group I : House Characteristics

Among the material used to build houses, only stone was a risk factor (Table B.I.1). Individuals whose walls were built of stone had 2.64 (c.i.: 1.27-5.48) times more risk of developing uta compared with the majority adobe, bricks or wood. This factor showed only in region 1 (OR = 2.54, c.i.: 1.22-5.29, $p < 0.01$), because in region 2 no houses were built of stone. In region 2 the comparison was made between adobe and bricks and no difference was detected. In addition, when walls were unfinished (no facing material) the risk of infection in a house was somewhat higher. The odds ratios among those who lived in houses with unfinished walls relative to those lived in houses with some facing were 1.46 (c.i.: 0.98-2.19, $p = 0.07$) in the whole study area and 1.68 (c.i.: 0.97-2.91, $p = 0.07$) in region 1 (Table C.I.1). In region 2, there was no evidence that wall-facing was important. Similar findings were obtained with covered floors. Because both variables differed in importance regionally, they were included in the multivariate analysis (MVA) below.

Several variables were used to evaluate the importance of windows in permiting the entry of sandflies into houses (Table A.I.1, A.I.3). Of these variables, holes in bedroom windows was the most significant (OR = 2.23, c.i.: 1.12-4.45). Existence of windows in the house (OR = 2.91, c.i.: 1.10-7.69) and house windows open (OR = 1.86, c.i.: 1.11-3.11) were remarkable only in region 2 (Table C.I.1). Considerable differences in both variables were observed between the two regions, and suggested interactions by region.

Having a chimney in a kitchen was a significant risk factor for uta (OR=1.99, c.i.: 1.19-3.34). Individuals living in houses with chimneys had a higher risk than those persons that lived in houses without chimneys (Tables B.I.1).

Table B.I.1 House Characteristics: Discrete Variables
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Variable	Case	Control	N	Matched Odds Ratio	Conf.limits Min - Max	P-value
Floor number						
2+	121	191	312	1.31	(0.89-1.93)	0.1856
1	66	144	210			
Total	187	335	522			
Room number						
1-3	98	170	268			
4-12	89	165	254	1.05	(0.72-1.53)	0.8705
Total	187	335	522			
Bedroom number						
1	100	158	258	1.31	(0.85-2.03)	0.2774
2+	87	177	264			
Total	187	335	522			
Floor cover						
Soil earth	145	240	385	1.53	(0.97-2.42)	0.0812
Cement & others	38	94	132			
Total	183	334	517			
Wall material						
Stone	24	19	43	2.64	(1.27-5.48)	0.0101
Adobe & clay	140	274	414			
Total	164	293	457			
Roof material						
Regional	40	66	106	1.26	(0.79-1.99)	0.3969
Modern	146	268	414			
Total	186	334	520			
Wall cover						
No cover	138	223	361	1.46	(0.98-2.19)	0.0759
Cover	48	109	157			
Total	186	332	518			
Windows in the house						
Yes	157	274	431	1.25	(0.75-2.10)	0.4619
No	30	61	91			
Total	187	335	522			
House Windows open						
1+	89	140	229	1.40	(0.95-2.08)	0.1134
0	98	195	293			
Total	187	335	522			

continuation B.I.1...

Variable	Case	Control	N	Matched Odds Ratio	Conf.limits Min - Max	P-value
Holes in house windows less bedrooms (sq cm)				1.92	(0.96-3.86)	0.0910
Yes	17	18	35			
No	170	317	487			
Total	187	335	522			
Holes in bedroom windows (sq cm)				2.23	(1.12-4.45)	0.0277
Yes	23	23	46			
No	164	312	476			
Total	187	335	522			
Daytime house lighting				1.54	(0.74-3.20)	0.3362
Dark	175	302	477			
Half light	12	33	45			
Total	187	335	522			
Daytime bedroom lighting				1.23	(0.77-1.96)	0.4491
Dark	149	253	402			
Half dark	38	82	120			
Total	187	335	522			
Kitchen location				0.90	(0.57-1.43)	0.7522
Inside	139	263	402			
Outside	48	72	120			
Total	187	335	522			
Chimney				1.99	(1.19-3.34)	0.0104
Yes	163	259	422			
No	24	76	100			
Total	187	335	522			
Latrine				1.59	(0.83-3.02)	0.1989
Yes	71	125	196			
No	116	210	326			
Total	187	335	522			

Table C.I.1. *Comparison of House Characteristics by Region*

Exposure	Region Lima + Ancash						Region Piura					
	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value
Floor number												
2+	64	104	168	1.05	0.59-1.88	0.9792	57	87	144	1.61	0.94-2.73	0.0993
1	26	43	69				40	101	141			
Total	90	147	237				97	188	285			
Room number												
1 - 3	60	101	161	0.89	0.51-1.55	0.7942	38	69	107	1.19	0.70-2.01	0.6001
4+	30	46	76				59	119	178			
Total	90	147	237				97	188	285			
Bedroom number												
1	69	109	178	1.12	0.62-2.02	0.8230	31	49	80	1.55	0.80-2.98	0.2733
2+	21	38	59				66	139	205			
Total	90	147	237				97	188	285			
Floor cover												
Soil earth	65	103	168	1.25	0.63-2.50	0.6458	80	137	217	1.79	0.97-3.30	0.0789
Cement & others	21	43	64				17	51	68			
Total	86	146	232				97	188	285			
Wall material												
Stone	24	19	43	2.54	1.22-5.29	0.0151	0	0	0	NA	NA	NA
Adobe & clay	45	93	138				95	181	276			
Total	69	112	181				95	181	276			
Roof material												
Regional	8	14	22	1.10	0.39-3.04	0.9340	32	52	84	1.34	0.79-2.25	0.3315
Foreing	82	133	215				64	135	199			
Total	90	147	237				96	187	283			
Wall cover												
No Cover	62	84	146	1.68	0.97-2.91	0.0784	76	139	215	1.33	0.72-2.45	0.4466
Cover	27	61	88				21	48	69			
Total	89	145	234				97	187	284			

continuation.....

Exposure	Region Lima + Ancash						Region Piura					
	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value
Windows in the house												
Yes	67	118	185	0.73	0.38-1.41	0.4316	90	156	246	2.91	1.10-7.69	0.0444
No	23	29	52				7	32	39			
Total	90	147	237				97	188	285			
House windows open												
Yes	24	45	69	0.88	0.46-1.69	0.8233	65	95	160	1.86	1.11-3.11	0.0236
No	66	102	168				32	93	125			
Total	90	147	237				97	188	285			
Holes in house windows less bedrooms												
Yes	2	0	2	NA	NA	NA	15	18	33	1.56	0.75-3.25	0.3178
No	87	147	234				82	170	252			
Total	89	147	237				97	188	285			
Holes in bedroom windows												
Yes	7	3	10	6.33	0.75-53.60	0.0932	16	20	36	1.68	0.78-3.62	0.2457
No	83	144	227				81	168	249			
Total	90	147	237				97	188	285			
Daytime house lighting												
Dark	87	141	228	1.05	0.25-4.39	0.7541	88	161	249	2.07	0.84-5.10	0.1864
Half light	3	6	9				9	27	36			
Total	90	147	237				97	188	285			
Daytime bedroom lighting												
Dark	78	119	197	1.50	0.71-3.17	0.3719	71	134	205	1.16	0.63-2.12	0.7618
Half light	12	28	40				26	54	80			
Total	90	147	237				97	188	285			
Kitchen location												
Inside	55	98	153	0.87	0.49-1.52	0.7165	84	165	249	0.99	0.43-2.25	0.8594
Outside	35	49	84				13	23	36			
Total	90	147	237				97	188	285			

continuation....

Exposure	Region Lima + Ancash						Region Piura					
	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value
Chimney												
Yes	76	110	186	1.85	0.90-3.79	0.1228	87	149	236	2.03	0.96-4.29	0.0871
No	14	37	51				10	39	49			
Total	90	147	237				97	188	285			
Latrine												
Yes	4	1	5	5.5	0.65-54.25	0.1813	67	124	191	1.36	0.69-2.69	0.4588
No	86	146	232				30	64	94			
Total	90	147	237				97	188	285			
Age of the house (yrs)												
0 - 7	17	26	43	1.20	0.60-2.38	0.7444	39	44	83	2.45	1.39-4.33	0.0035
7.1+	73	121	194				58	144	202			
Total	90	147	237				97	188	285			
Length of occupation the house (yrs)												
0 - 6	56	95	151	0.89	0.41-1.92	0.9225	67	120	187	1.70	0.80-3.61	0.2336
6.1+	34	52	86				30	68	98			
Total	90	147	237				97	188	285			
Bedroom size (sq m)												
0 - 25	59	87	146	1.31	0.75-2.29	0.3974	67	109	176	1.53	0.91-2.59	0.1302
25.1+	31	60	91				30	79	109			
Total	90	147	237				97	188	285			
Distance to kitchen (m)												
4+	19	18	37	1.79	0.86-3.74	0.1813	4	3	7	1.79	0.38-8.49	0.7175
0 - 4	71	129	200				93	185	278			
Total	35	49	237				97	188	285			
Distance to latrine (m)												
0 - 10	88	147	235	NA	NA	NA	80	141	221	1.58	0.84-2.96	0.1847
10.1+	2	0	2				17	47	64			
Total	90	147	237				97	188	285			

Table D.I.1. Comparison of House Characteristics in Children and Adults

Exposure	Children						Adults					
	Case	Control	Total	Matched Odds Ratio	Confidence Limits	P-value	Case	Control	Total	Matched Odds Ratio	Confidence Limits	P-value
Floor number												
2+	102	166	268	1.34	0.88-2.04	0.1889	19	25	44	1.19	0.41-3.46	0.9632
1	55	125	180				11	19	30			
Total	157	291	448				30	44	74			
Room number												
1 - 3	82	150	232	0.97	0.64-1.46	0.9569	16	20	36	1.40	0.53-3.71	0.6692
4+	75	141	216				14	24	38			
Total	157	291	448				30	44	74			
Bedroom number												
1	86	135	221	1.40	0.87-2.27	0.2128	14	23	37	0.93	0.31-2.77	0.8927
2+	71	156	227				16	21	37			
Total	157	291	448				30	44	74			
Floor cover												
Soil earth	121	211	332	1.43	0.87-2.35	0.1886	24	29	53	2.22	0.57-8.60	0.3619
Cement & others	33	79	112				5	15	20			
Total	154	290	444				29	44	73			
Wall material												
Stone	18	14	32	3.00	1.23-7.30	0.0184	6	5	11	2.00	0.55-7.29	0.445
Adobe & clay	120	241	361				20	33	53			
Total	138	255	393				26	38	64			
Roof material												
Regional	36	61	97	1.22	0.74-2.00	0.5170	4	5	9	1.36	0.36-5.12	0.9074
Foreing	120	229	349				26	39	65			
Total	156	290	446				30	44	74			
Wall cover												
No Cover	118	194	312	1.58	1.01-2.47	0.0508	20	29	49	1.26	0.42-3.82	0.8891
Cover	38	94	132				10	15	25			
Total	156	288	444				30	44	74			

continuation.....

Exposure	Children Case	Children Control	Children Total	Children Matched Odds Ratio	Children Confidence Limits	Children P-value	Adults Case	Adults Control	Adults Total	Adults Matched Odds Ratio	Adults Confidence Limits	Adults P-value
Windows in the house												
Yes	133	238	371	1.41	0.79-2.53	0.3082	24	36	60	0.77	0.24-2.43	0.8735
No	24	53	77				6	8	14			
Total	157	291	448				30	44	74			
House windows open												
1+	73	120	193	1.46	0.94-2.25	0.1178	16	20	36	1.41	0.55-3.64	0.6253
None	84	171	255				14	24	38			
Total	157	291	448				30	44	74			
Holes in house windows less bedrooms												
Yes	12	17	29	1.53	0.70-3.37	0.3858	5	1	6	8.50	0.96-75.07	0.0929
No	145	274	419				25	43	68			
Total	157	291	448				30	44	74			
Holes in bedroom windows												
Yes	19	18	37	2.70	1.25-5.84	0.0152	4	5	9	1.14	0.20-6.66	0.7604
No	138	273	411				26	39	65			
Total	157	291	448				30	44	74			
Daytime house lighting												
Dark	145	262	407	1.31	0.62-2.78	0.6132	30	40	70	NA	NA	NA
Half light	12	29	41				0	4	4			
Total	157	291	448				30	44	74			
Daytime bedroom lighting												
Dark	124	217	341	1.19	0.73-1.95	0.5676	25	36	61	1.06	0.22-5.12	0.7603
Half light	33	74	107				5	8	13			
Total	157	291	448				30	44	74			
Kitchen location												
Inside	119	232	351	0.84	0.51-1.40	0.5886	20	31	51	1.14	0.37-3.48	0.9601
Outside	38	59	97				10	13	23			
Total	157	291	448				30	44	74			

continuation....

Exposure	Children						Adults					
	Case	Control	Total	Matched Odds Ratio	Confidence Limits	P-value	Case	Control	Total	Matched Odds Ratio	Confidence Limits	P-value
Chimney												
Yes	140	229	369	2.20	1.21-4.03	0.0120	23	30	53	1.59	0.53-4.79	0.5726
No	17	62	79				7	14	21			
Total	157	291	448				30	44	74			
Latrine												
Yes	64	117	181	1.53	0.75-3.12	0.3061	7	8	15	1.40	0.19-10.39	0.8773
No	93	174	267				23	36	59			
Total	157	291	448				30	44	74			
Age of the house (yrs)												
0 - 7	49	65	114	1.59	1.01-2.50	0.0618	7	5	12	2.92	0.66-12.91	0.2654
7.1+	108	226	334				23	39	62			
Total	157	291	448				30	44	74			
Length of occupation the house (years)												
0 - 6	114	203	317	1.16	0.62-2.16	0.7581	9	12	21	1.35	0.48-3.78	0.7439
6.1+	43	88	131				21	32	53			
Total	157	291	448				30	44	74			
Bedroom size (sqm)												
0 - 25	110	177	287	1.46	0.96-2.21	0.0786	16	19	35	1.75	0.65-4.72	0.3924
25.1+	47	114	161				14	25	39			
Total	157	291	448				30	44	74			
Distance to kitchen (m)												
4+	141	248	389	1.60	0.89-3.86	0.1424	5	4	9	2.07	0.46-9.37	0.5537
0 - 4	16	43	59				25	40	65			
Total	157	291	448				30	44	74			
Distance to latrine (m)												
0 - 10	141	248	389	1.60	0.84-3.05	0.1883	27	40	67	2.00	0.24-16.46	0.8638
10.1+	16	43	59				3	4	7			
Total	157	291	448				30	44	74			

The risk of developing uta was higher among individuals whose houses had small bedrooms (equal to or less than 25 square meters) [OR = 1.47, c.i.: 1.0-2.15]. Also, individuals living in houses seven years old or less were at greater risk (OR = 1.76, c.i.: 1.15-2.70) (Table B.I.2).

Group II : Features Around the House

The odds ratio for developing uta among those persons who lived in houses close to creeks (< 100 meters) or close to waterways (< 30 meters) was 1.8 and 2.8 respectively. By contrast, proximity to a road or a river was protective (Table B.II.1). Considerable variation in the importance of these factors was observed by region. Important in region 1 were proximity to creeks as a risk factor (OR = 3.19, c.i.: 1.22-8.36) and to road as a protective factor (OR = 2.64, c.i.: 1.27-5.48). In region 2, proximity to waterways as a risk factor (OR = 2.82, c.i.: 1.57-5.07), and to rivers as a protective factor (OR = 4.59, c.i.: 1.87-11.25) were important (Table C.II.1). In addition, the existence of a neighbouring kitchen garden was a risk factor in region 2 (OR = 2.36, c.i.: 1.14-4.86). Similarly, there were differences in risk factors by age group (Table D.II.1). Creeks (OR = 1.94, c.i: 1.13-3.32), waterways (OR = 1.79, c.i.: 1.12-2.87) and rivers (OR = 3.91 as a protected factor, c.i.: 1.72-8.89) were apparently important for persons under 15 years, while a neighbouring kitchen garden (OR = 4.06, c.i.: 1.06-15.52) was important for adults (Table D.II.1). The data suggest that these differences are not real, because of the small sample size in the strata of adults (Table D.II.1). The proximity and extent of dry stone walls and plants around the houses had no significance for risk of the disease in this study.

Group III: Human Indoor Behaviour

Because the analysis of human indoor behaviour is complex, the variables in this group were divided into four subgroups : house

Table B.I.2 House Characteristics: Continuous Variables
Case-Control study on Cutaneous Leishmaniasis, Peru 1991-1992

Variable	Case	Control	N	Matched Odds Ratio	Conf.limits Min - Max	P-value
Age of the house (yrs)						
0 - 7	56	70	126	1.76	(1.15-2.70)	0.0148
7+	131	265	396			
Total	187	335	522			
Lenght of occupation the house (yrs)						
0 - 6	123	215	338	1.27	(0.75-2.15)	0.4606
6+	64	120	184			
Total	187	335	522			
Bedrooms size (sq m)						
25+	126	196	322	1.47	(1.00-2.15)	0.0495
0 - 25	61	139	200			
Total	187	335	522			
Distance to kitchen (m)						
4+	23	21	44	1.89	(0.98-3.66)	0.0804
0 - 4	164	314	478			
Total	187	335	522			
Distance to latrine (m)						
10+	168	288	456	1.52	(0.78-2.58)	0.3021
0 - 10	19	47	66			
Total	187	335	522			

Table B.II.1 Features Around the House
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Variable	Case	Control	N	Matched Odds Ratio	Conf.limits Min - Max	P-value
Distance to hill (m)						
1 - 30	93	160	253	1.22	(0.75-1.97)	0.4899
30+	94	175	269			
Total	187	335	522			
Distance to creeks (m)						
1 - 100	55	74	129	1.83	(1.10-3.03)	0.0294
100+	132	261	393			
Total	187	335	522			
Distance to road (m)						
30+	91	121	212	1.88	(1.24-2.86)	0.0022
1 - 30	96	214	310			
Total	187	335	522			
Distance to river (m)						
30+	174	282	456	2.81	(1.37-5.76)	0.0047
1 - 30	13	53	66			
Total	187	335	522			
Distance to waterways (m)						
1 - 200	97	146	243	1.74	(1.14-2.68)	0.0124
200+	89	187	276			
Total	186	333	519			
Distance to kitchen garden (m)						
100+	102	151	253	1.49	(0.98-2.27)	0.0810
1 - 100	85	184	269			
Total	187	335	522			
Distance to neighbouring kitchen garden (m)						
1 - 80	58	86	144	1.43	(0.91-2.25)	0.1248
80+	129	249	378			
Total	187	335	522			
Distance to stone walls (m)						
1 - 80	95	160	255	1.08	(0.73-1.62)	0.7694
80+	92	175	267			
Total	187	335	522			
Presence of stone walls						
Yes	95	160	255	1.08	(0.73-1.62)	0.7694
No	92	175	267			
Total	187	335	522			

Table C.II.1. Comparison of Features Around the House by Region

Exposure	Region Lima + Ancash						Region Piura					
	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value
Distance to hill (m)												
1 - 30	76	126	202	1.04	0.4-2.69	0.8732	70	131	201	1.23	0.64-2.34	0.6384
30+	14	21	35				27	57	84			
Total	90	147	237				97	188	285			
Distance to creeks (m)												
1 - 100	21	23	44	3.19	1.22-2.36	0.0199	34	51	85	1.52	0.81-2.85	0.2677
100+	69	124	193				63	137	200			
Total	90	147	237				97	188	285			
Distance to road (m)												
30+	42	46	88	2.64	1.27-5.48	0.0109	49	75	124	1.61	0.95-2.72	0.0766
1 - 30	48	101	149				48	113	161			
Total	90	147	237				97	188	285			
Distance to river (m)												
30+	86	143	229	0.90	0.19-4.24	0.7946	88	139	227	4.59	1.87-11.25	0.0005
1 - 30	4	4	8				9	49	58			
Total	90	147	237				97	188	285			
Distance to waterways (m)												
1 - 200	45	82	127	0.92	0.47-1.81	0.9530	52	64	116	2.82	1.57-5.07	0.0007
200+	44	65	109				45	122	167			
Total	89	147	236				97	186	283			
Distance to kitchen garden (m)												
100+	56	80	136	1.62	0.83-3.16	0.2068	46	71	117	1.58	0.90-2.77	0.1497
1 - 100	34	67	101				51	117	168			
Total	90	147	237				97	188	285			
Distance to neighbouring kitchen garden (m)												
1 - 80	32	57	89	1.02	0.57-1.84	0.9372	26	29	55	2.36	1.14-4.86	0.0234
80+	58	90	148				71	159	230			
Total	90	147	237				97	188	285			
Distance to stone walls (pircas)												
1 - 80	65	93	158	1.43	0.78-2.63	0.3163	30	67	97	0.82	0.48-1.43	0.5733
80+	25	54	79				67	121	188			
Total	90	147	237				97	188	285			

Table D.II.1. Comparison of Features Around the Hopuse in Children and Adults

Exposure	Children Case	Children Control	Children N	Children Matched Odds Ratio	Children Confidence Limits	Children P-value	Adults Case	Adults Control	Adults N	Adults Matched Odds Ratio	Adults Confidence Limits	Adults P-value
Distance to hill (m)												
1 - 30	128	229	357	1.34	0.74-2.42	0.4112	18	28	46	0.92	0.24-3.60	0.8173
30+	29	62	91				12	16	28			
Total	157	291	448				30	44	74			
Distance to creeks (m)												
1 - 100	49	65	114	1.94	1.13-3.32	0.0249	6	9	15	1.67	0.29-9.67	0.8875
100+	108	226	334				24	35	59			
Total	157	291	448				30	44	74			
Distance to road (m)												
30+	78	108	186	1.83	1.17-2.86	0.0074	13	13	26	1.71	0.51-5.71	0.5679
1 - 30	79	183	262				17	31	48			
Total	157	291	448				30	44	74			
Distance to river (m)												
30+	147	239	386	3.91	1.72-8.89	0.0007	27	43	70	NA	NA	NA
1 - 30	10	52	62				3	1	4			
Total	157	291	448				30	44	74			
Distance to waterways (m)												
1 - 200	83	127	210	1.79	1.12-2.87	0.0169	14	19	33	2.18	0.66-7.19	0.3381
200+	73	162	235				16	25	41			
Total	156	289	445				30	44	74			
Distance to kitchen garden (m)												
100+	86	131	217	1.58	0.98-2.53	0.0737	16	20	36	1.47	0.51-4.27	0.656
1 - 100	71	160	231				14	24	38			
Total	157	291	448				30	44	74			
Distance to neighbouring kitchen garden (m)												
1 - 80	46	76	122	1.24	0.75-2.03	0.4464	12	10	22	4.06	1.06-15.52	0.0457
80+	111	215	326				18	34	52			
Total	157	291	448				30	44	74			
Distance to pircas (m)												
1 - 80	80	137	217	1.12	0.73-1.71	0.6833	15	23	38	0.97	0.28-3.31	0.8023
80+	77	154	231				15	21	36			
Total	157	291	448				30	44	74			

modification, illumination of the house at night, stored products in the house and animals or plants around the house.

Individuals who modified their houses (within one year prior to the admission date) had greater risk of developing uta (OR = 1.89, ci.: 1.15-3.09) compared with those persons who made no modifications (Table B.III.1). It was not possible to determine if any specific type of modification (i.e. construction or repair of walls, floors, roofs, etc) represented a risk because the sample size in every category was small (Table A.III.1). Modification of the house suggested a higher risk to children than adults but the small sample size (wide confident limits) did not permit a definitive conclusion (Table D.III.1).

No differences in the risk of uta were found by length of residency in a house, number of residents, or insecticide spray application (within six months of the admission date). This was true for the whole study population, and by region and age group (Tables B.III.1, C.III.1, and D.III.1).

Intensity of illumination at night was a risk factor by region, but not in the whole study area (Tables C.III.1, B.III.1). In region 1, individuals who used home-made lamps were at greater risk of developing uta (OR = 2.88, c.i.: 1.16-7.16) than those who used other kinds of lights at night. No differences were observed in region 2. Those persons who used "petromax" lights (highest intensity) were excluded from this analysis because of the small number of users. On the other hand, in region 1 the use of proprietary lamps was a protective factor. Individuals who used this type of lamp were at lower risk of acquiring the disease in comparison with persons that used other kinds of lamps (OR = 3.50, c.i.: 1.48-8.29). Notice that in this last case comparison was made with those persons that used any other type of light. In other words, a home-made lamp represents a risk (lamps without a glass tube). No difference between cases and controls was found according to daytime illumination (Tables B.I.1, C.I.1 and D.I.1).

For products stored in the house, only wood was detected as a potential risk factor (Table B.III.2): individuals keeping wood in their houses had a higher risk of developing uta than those persons who did not (OR =

Table B.III.1 Human Indoor Behaviour
Case-Control study on Cutaneous Leishmaniasis, Peru 1991-1992

Variable	Case	Control	N	Matched Odds Ratio	Conf.limits Min - Max	P-value
Time living in the house (yrs)						
1 - 5	108	179	235	1.49	(0.91-2.45)	0.1447
5.1+	79	156	287			
Total	187	335	522			
House modification (< 1 year)						
Yes	38	45	83	1.89	(1.15-3.09)	0.0141
No	149	290	439			
Total	187	335	522			
Sprayed insecticide in the house (< 1 year)						
Yes	24	49	73	0.69	(0.38-1.27)	0.2758
No	163	286	449			
Total	187	335	522			
Number of residents						
7+	116	195	311	1.25	(0.85-1.84)	0.3123
1 - 6	71	140	211			
Total	187	335	522			
Candles						
Yes	178	317	495	1.14	(0.47-2.76)	0.9418
No	9	18	27			
Total	187	335	522			
Home-made kerosene lamp						
Yes	99	170	269	1.17	(0.75-1.84)	0.5658
No	88	165	253			
Total	187	335	522			
Proprietary kerosene lamp						
No	89	134	223	1.44	(0.96-2.18)	0.0888
Yes	97	200	297			
Total	186	334	520			

Table C.III.1. Comparison of Human Indoor Behaviour by Region

Exposure	Region Lima + Ancash						Region Piura					
	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value
Length of occupation the house												
1 - 60	50	79	129	1.23	0.61-2.48	0.6933	58	100	158	1.98	0.95-4.16	0.0975
61+	40	68	108				39	88	127			
Total	90	147	237				97	188	285			
House modification (< 1 year)												
Yes	13	15	28	1.74	0.78-3.85	0.2546	25	30	55	1.89	1.00-3.58	0.0616
No	77	132	209				72	158	230			
Total	90	147	237				97	188	285			
Sprayed insectice (< 1 year)												
Yes	22	38	60	0.78	0.40-1.51	0.5415	2	11	13	0.42	0.09-1.95	0.408
No	68	109	177				95	177	272			
Total	90	147	237				97	188	285			
Number of residents												
7+	52	62	114	1.92	1.12-3.28	0.0184	64	133	197	0.79	0.43-1.46	0.5786
1 - 6	38	85	123				33	55	88			
Total	90	147	237				97	188	285			
Candles												
Yes	82	129	211	1.33	0.53-3.37	0.7094	96	188	284	NA	NA	NA
No	8	18	26				1	0	1			
Total	90	147	237				97	188	285			
Home-made kerosene lamp												
Yes	36	38	74	2.88	1.16-7.16	0.0443	63	132	195	0.84	0.49-1.43	0.6165
No	54	109	163				34	56	90			
Total	90	147	237				97	188	285			
Proprietary kerosene lamp												
No	38	36	74	3.50	1.48-8.29	0.0064	51	98	149	1.03	0.63-1.66	0.9832
Yes	52	111	163				45	89	134			
Total	90	147	237				96	187	283			
Stored products in house												
Yes	85	133	218	1.39	0.49-3.97	0.7084	82	164	246	0.76	0.37-1.58	0.5997
No	5	14	19				15	24	39			
Total	90	147	237				97	188	285			

continuation...

Seeds													
Yes		37	57	94	1.14	0.60-2.16	0.8010	23	40	63	1.16	0.63-2.16	0.756
No		53	90	143				74	148	222			
	Total	90	147	237				97	188	285			
Grains													
Yes		13	21	34	1.11	0.54-2.28	0.9251	20	27	47	1.65	0.86-3.15	0.1884
No		77	126	203				77	161	238			
	Total	90	147	237				97	188	285			
Tubercles													
Yes		31	50	81	1.02	0.54-1.92	0.9149	91	169	260	1.83	0.69-4.83	0.3014
No		59	97	156				6	19	25			
	Total	90	147	237				97	188	285			
Wood													
Yes		11	6	17	4.83	1.24-18.80	0.0466	5	6	11	1.55	0.43-5.58	0.7404
No		79	141	220				92	182	274			
	Total	90	147	237				97	188	285			
Cows													
Yes		7	7	14	1.83	0.64-5.22	0.3709	13	14	27	1.96	0.83-4.60	0.1556
No		83	140	223				84	174	258			
	Total	90	147	237				97	188	285			
Goats													
Yes		15	30	45	0.72	0.33-1.56	0.5177	20	24	44	1.87	0.97-3.60	0.087
No		75	117	192				77	164	241			
	Total							97	188	285			
Sheeps													
Yes		30	31	61	1.95	1.02-3.72	0.061	12	23	35	0.96	0.45-2.06	0.924
No		60	116	176				85	165	250			
	Total	90	147	237				97	188	285			
Chickens													
Yes		38	53	91	1.46	0.80-2.66	0.2804	18	24	42	1.68	0.82-3.44	0.2139
No		52	94	146				79	164	243			
	Total	90	147	237				97	188	285			
Dogs													
Yes		27	46	73	1.05	0.56-2.00	1.000	58	93	151	1.72	1.00-2.96	0.0671
No		63	101	164				39	95	134			
	Total	90	147	237				97	188	285			

Table D.III.1 Comparison of Human Indoor Behaviour by Age Group

Exposure	Children						Adults					
	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value
Length of occupation the house												
1 - 60	99	168	267	1.42	0.80-2.53	0.2957	9	11	20	1.51	0.56-4.12	0.559
61+	58	123	181				21	33	54			
Total	157	291	448				30	44	74			
House modification (< 1 year)												
Yes	33	39	72	1.99	1.15-3.45	0.0166	5	6	11	1.52	0.46-5.05	0.7102
No	124	252	376				25	38	63			
Total	157	291	448				30	44	74			
Sprayed insectice (< 1 year)												
Yes	18	39	57	0.66	0.34-1.29	0.2602	6	10	16	0.88	0.21-3.70	0.8613
No	139	252	391				24	34	58			
Total	157	291	448				30	44	74			
Number of residents												
7+	101	175	276	1.30	0.84-2.02	0.2813	15	20	35	1.09	0.45-2.62	0.9699
1 - 6	56	116	172				15	24	39			
Total	157	291	448				30	44	74			
Candles												
Yes	150	276	426	1.19	0.43-3.28	0.9358	28	41	69	1.00	0.16-6.14	0.6069
No	7	15	22				2	3	5			
Total	157	291	448				30	44	74			
Home-Made kerosene lamp												
Yes	79	142	221	1.16	0.72-1.89	0.6241	20	28	48	0.83	0.20-3.55	0.9035
No	78	149	227				10	16	26			
Total	157	291	448				30	44	74			
Proprietary kerosene lamp												
Yes	70	110	180	1.40	0.91-2.17	0.1453	19	24	43	1.64	0.44-6.14	0.6606
No	86	180	266				11	20	31			
Total	156	290	446				30	44	74			
Stored products in house												
Yes	140	256	396	1.06	0.56-2.00	0.9792	27	41	68	0.59	0.12-3.02	0.8299
No	17	35	52				3	3	6			
Total	157	291	448				30	44	74			

continuation....

Seeds													
Yes		46	85	131	0.90	0.55-1.48	0.7724	14	12	26	3.23	0.98-10.66	0.0533
No		111	206	317				16	32	48			
	Total	157	291	448				30	44	74			
Grains													
Yes		28	45	73	1.18	0.71-1.96	0.6158	5	3	8	2.62	0.59-10.57	0.3586
No		129	246	375				25	41	66			
	Total	157	291	448				30	44	74			
Tuber													
Yes		104	195	299	1.13	0.65-1.97	0.7818	18	24	42	2.13	0.50-8.97	0.4884
No		53	96	149				12	20	32			
	Total	157	291	448				30	44	74			
Wood													
Yes		13	10	23	3.00	1.08-8.36	0.0604	3	2	5	2.50	0.39-16.05	0.6434
No		144	281	425				27	42	69			
	Total	157	291	448				30	44	74			
Cows													
Yes		16	19	35	1.69	0.82-3.51	0.2031	4	2	6	2.50	0.44-14.30	0.4753
No		141	172	413				26	42	68			
	Total	157	291	448				30	44	74			
Goats													
Yes		31	52	83	1.19	0.71-2.01	0.5903	4	2	6	2.80	0.51-15.5	0.4008
No		126	139	365				26	42	68			
	Total	157	291	448				30	44	74			
Sheeps													
Yes		34	45	79	1.54	0.91-2.60	0.1433	8	9	17	1.71	0.56-5.29	0.5193
No		123	246	369				22	35	57			
	Total	157	291	448				30	44	74			
Chickens													
Yes		47	62	109	1.75	1.06-2.91	0.036	9	15	24	0.76	0.23-2.51	0.8806
No		110	229	339				21	29	50			
	Total	157	291	448				30	44	74			
Dogs													
Yes		24	53	77	0.70	0.37-1.32	0.3526	12	14	26	2.05	0.56-4.52	0.5328
No		133	238	371				18	30	48			
	Total	157	291	448				30	44	74			

2.88, c.i.: 1.18-7.06). This was true only in region 1 [OR = 4.83, c.i.: 1.24-18.80] (Table C.III.1). A large number of products were investigated, analyzing by groups of products and families of plants, with no other significant result.

Plants and domestic animals around the dwellings were searched by species and family. Tables B.III.3, C.III.1 and D.III.1 condense the principal results; none was a risk factor associated with the transmission of uta. Because the dog has been reported as a suspected reservoir of Andean cutaneous leishmaniasis, special effort was made to explore its role, but we could find no significant evidence that dogs were associated with the transmission of this disease. Goats, however, had an OR of 1.87 (c.i.: 0.97-3.60, $p = 0.08$) in region 2 and the OR of sheep was 1.95 (c.i.: 1.0-3.72, $p = 0.06$) in region 1, and of cows 1.81 (c.i.: 0.94-3.47) in the whole study area.

Group IV : Human Outdoor Behaviour

Because a high percentage of persons reported no exposure to the majority of variables of this group (Tables B.IV.1, B.IV.2), these were analyzed as dichotomous (exposed vs not exposed) variables. Those persons not owning land were excluded in the analysis of number of plots.

Only work at night on irrigation (usually by periods between 8 to 12 hours) gave a significant OR (2.96, c.i.: 1.37-6.36). Sleeping at a plot gave OR = 1.57 (c.i.: 1.00 - 2.48) close to significance ($p = 0.055$), and an unmatched analysis of this factor showed a positive trend ($p = 0.03$) when categorized for number of nights slept at plot (values 0, 1 and 2). Sleeping at a plot at night and working at night on irrigation showed significant differences in their ORs between regions (Table C.IV.1). The former was significantly higher in region 1 than in region 2 and the latter was significant in region 2 but not in region 1, perhaps because the number of individuals engaged in these activities was lower.

Children were at greater risk when they participated (jointly with their parents) in irrigation of the crops at night, or worked in creeks ($p < 0.05$,

Table B.III.2 Human Indoor Behaviour: Products Stored in House
Case-Control study on Cutaneous Leishmaniasis, Peru 1991-1992

Variable	Case	Control	N	Matched Odds Ratio	Conf.limits Min - Max	P-value
Stored products in house						
Yes	167	297	464	0.97	(0.54-1.75)	0.9608
No	20	38	58			
Total	187	335	522			
Seeds						
No	60	97	157	1.14	(0.73-1.77)	0.6386
Yes	127	238	365			
Total	187	335	522			
Grains						
No	33	48	81	1.30	(0.81-2.09)	0.3441
Yes	154	287	441			
Total	187	335	522			
Tuber						
No	122	219	341	1.18	(0.71-1.97)	0.6119
Yes	65	116	181			
Total	187	335	522			
Fruits						
Yes	17	17	34	2.12	(0.95-4.75)	0.0889
No	170	318	488			
Total	187	335	522			
Wood						
Yes	16	12	28	2.88	(1.18-7.06)	0.0363
No	171	323	494			
Total	187	335	522			
Green vegetable						
Yes	16	26	42	1.14	(0.57-2.28)	0.8582
No	171	309	480			
Total	187	335	522			
Other products						
No	179	318	497	1.14	(0.45-2.87)	0.9685
Yes	8	17	25			
Total	187	335	522			

Table B.III.3 Human Indoor Behaviour : Domestic Animals
Case-Control study on Cutaneous Leishmaniasis, Peru 1991-1992

Variable	Case	Control	N	Matched Odds Ratio	Conf.limits Min - Max	P-value
Guinea pigs						
No	108	171	279	1.26	(0.87-1.83)	0.2586
Yes	79	164	243			
Total	187	335	522			
Cows						
Yes	20	21	41	1.81	(0.94-3.47)	0.0888
No	167	314	481			
Total	187	335	522			
Horses						
Yes	46	84	130	1.05	(0.67-1.66)	0.9064
No	141	251	392			
Total	187	335	522			
Goats						
Yes	35	54	89	1.26	(0.77-2.06)	0.4203
No	152	281	433			
Total	187	335	522			
Sheep						
Yes	42	54	96	1.55	(0.97-2.49)	0.0937
No	145	281	426			
Total	187	335	522			
Pigs						
Yes	80	144	224	1.04	(0.68-1.59)	0.9569
No	107	191	298			
Total	187	335	522			
Chickens						
No	56	77	133	1.46	(0.93-2.30)	0.1277
Yes	131	258	389			
Total	187	335	522			
Cats						
No	157	267	424	1.79	(0.89 -2.85)	0.1631
Yes	30	68	98			
Total	187	335	522			
Dogs						
No	85	139	224	0.77	(0.51-1.15)	0.2298
Yes	102	196	298			
Total	187	335	522			

Table B.IV.1 Human Outdoor Behaviour
Case-Control Study on Cutaneous Leishmaniasis, Peru 1990-1992

Variable	Case	Control	N	Matched Odds Ratio	Conf.limits Min - Max	P-value
Repairing waterways						
Yes	20	21	41	1.77	(0.92-3.43)	0.1042
No	167	314	481			
Total	187	335	522			
Repairing roads						
No	181	323	504	1.20	(0.43-3.39)	0.9326
Yes	6	12	18			
Total	187	335	522			
Repairing or building pircas						
No	177	315	492	1.28	(0.54-2.99)	0.7223
Yes	10	20	30			
Total	187	335	522			
Weeding						
Yes	89	139	228	1.31	(0.87-1.97)	0.2304
No	98	196	294			
Total	187	335	522			
Cutting wood						
Yes	33	43	76	1.61	(0.92-2.82)	0.1284
No	154	292	446			
Total	187	335	522			
Irrigation work at night						
Yes	23	19	42	2.96	(1.37-6.36)	0.0085
No	164	316	480			
Total	187	335	522			

Table B.IV.2 Human Outdoor Behavior : Crops
Case-Control Study on Cutaneous Leishmaniasis, Peru 1990-1992

Variable	Case	Control	N	Matched Odds Ratio	Conf.limits Min - Max	P-value
Number of plots						
Yes	159	267	426	1.70	(0.95-3.05)	0.0956
No	28	68	96			
Total	187	335	522			
Days in plots (< 3 months)						
Yes	152	253	405	1.71	(0.99-2.98)	0.0753
No	35	82	117			
Total	187	335	522			
Occasions slept at plot (< 3 months)						
Yes	55	71	126	1.57	(1.00-2.48)	0.0559
No	132	264	396			
Total	187	335	522			
Number of plots on creeks						
Yes	70	101	171	1.33	(0.88-2.01)	0.1910
No	117	234	351			
Total	187	335	522			
Days in creeks (< 3 months)						
Yes	59	80	139	1.49	(0.97-2.31)	0.0859
No	128	255	383			
Total	187	335	522			
Number of plots on slopes						
Yes	138	238	376	1.24	(0.78-1.99)	0.4268
No	49	97	146			
Total	187	335	522			
Days in slopes (< 3 months)						
Yes	129	226	355	1.13	(0.72-1.78)	0.6842
No	58	109	167			
Total	187	335	522			
Number of plots elsewhere						
Yes	11	23	34	0.86	(0.41-1.81)	0.8269
No	176	312	488			
Total	187	335	522			
Days in elsewhere (< 3 months)						
No	177	314	491	1.12	(0.52-2.39)	0.9241
Yes	10	21	31			
Total	187	335	522			

Table D.IV.1). OR's were not available for work on hillsides or at other location, because of the small number of pairs for the matched analysis (Table D.IV.1).

As with the previous groups, the majority of OR's vary between regions and age groups but, frequently, the confidence limits were wide because of the sample size and/or interactions which might be present (Tables C.IV.1, C.IV.2, D.IV.1 and D.IV.2).

Table B.V.1 summarizes the more important variables emerging from the matched analysis ($p < 0.05$ in both pooled and/or by region and/or age group).

Because this was a concurrent case-control study the frequency of variables in controls should be very close to the distribution of these factors in the general population (Rothman 1986, Wacholder *et al.* 1992b). Figures 9 to 15 show the distribution of selected variables in controls from the Table B.V.1. Several dichotomous characteristics of houses (Figure 9) as well as indoor and outdoor behaviours (Figure 10) have distinct distributions between regions 1 and 2 ($p < 0.01$). Similarly, some continuous variables (Figures 12 to 14) have greater frequency only in one region ($p < 0.001$). The more important differences by age ($p < 0.001$) were work activities: reparing waterways, in irrigation at night and on crops located on creeks (Figure 15).

As part of the preliminary inspection of the relationships between potential risk factors and their interdependence (confounding effect), a gross cross-correlation was tried separately for each region (Appendices 4 and 5). This correlation ignores, for practical reasons, the discrete or non-normal nature of some of the variables. The intention is merely to point towards possible co-linear variables which may suggest explanations for the appearance or disappearance of terms in the final multivariate model. As can be seen in Appendices 4 and 5 most of the variates are not strongly associated.

Table C.IV.1. Comparison of Human Outdoor Behaviour by Region

Exposure	Region Lima + Ancash: Case	Control	N	Matched Odds Ratio	Confidence Limitis	P-value	Region Piura: Case	Control	N	Matched Odds Ratio	Confidence Limitis	P-value
Repairing waterways												
Yes	11	10	21	1.82	0.75-4.40	0.2471	9	11	20	1.72	0.64-4.62	0.3786
No	79	137	216				88	177	265			
Total	90	147	237				97	188	285			
Repairing roads												
No	87	139	226	1.67	0.38-7.22	0.7404	94	184	278	0.82	0.18-3.70	0.8955
Yes	3	8	11				3	4	7			
Total	90	147	237				97	188	285			
Repairing stone walls												
No	81	135	216	0.80	0.29-2.19	0.8580	96	180	276	4.25	0.55-32.70	0.2418
Yes	9	12	21				1	8	9			
Total	90	147	237				97	188	285			
Weeding												
Yes	46	66	112	1.22	0.69-2.17	0.5958	43	73	116	1.31	0.73-2.34	0.4566
No	44	81	125				54	115	169			
Total	90	147	237				97	188	285			
Cutting wood												
Yes	11	7	18	2.92	1.05-8.15	0.0639	22	36	58	1.19	0.59-2.41	0.7675
No	79	140	219				75	152	227			
Total	90	147	237				97	188	285			
Irrigation work at night												
Yes	13	8	21	3.73	1.27-10.92	0.0235	10	11	21	2.25	0.74-6.88	0.2589
No	77	139	216				87	177	264			
Total	90	147	237				97	188	285			

Table D.IV.1. Comparison of Human Outdoor Behaviour By Age

Exposure	Children						Adults					
	Case	Control	N	Matched Odds Ratio	Confidence Limitis	P-value	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value
Repairing waterways												
Yes	13	11	24	2.19	0.93-5.17	0.1019	7	10	17	1.21	0.42-3.46	0.9266
No	144	280	424				23	34	57			
Total	157	291	448				30	44	74			
Repairing roads												
No	155	286	441	1.38	0.28-6.86	1.0000	26	37	63	1.80	0.28-4.24	0.8262
Yes	2	5	7				4	7	11			
Total	157	291	448				30	44	74			
Repairing stone walls												
No	151	278	429	1.09	0.40-2.98	0.9306	26	37	63	1.29	0.23-7.28	0.8875
Yes	6	13	19				4	7	11			
Total	157	291	448				30	44	74			
Weeding												
Yes	69	114	183	1.23	0.80-1.89	0.4016	20	25	45	2.38	0.56-10.11	0.3855
No	88	177	265				10	19	29			
Total	157	291	448				30	44	74			
Cutting wood												
Yes	24	34	58	1.57	0.85-2.93	0.1963	9	9	18	2.50	0.54-11.60	0.4635
No	133	257	390				21	35	56			
Total	157	291	448				30	44	74			
Irrigation work at night												
Yes	15	12	27	3.36	1.30-8.68	0.0225	8	7	15	2.14	0.47-9.72	0.5443
No	142	279	421				22	37	59			
Total	157	291	448				30	44	74			

Table C.IV.2 Comparison of Human Outdoor Behaviour by Region: Crops

Exposure	Region Lima + Ancash						Region Piura					
	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value
Number of plots												
Yes	76	119	195	1.92	0.73-5.08	0.2557	83	148	231	1.78	0.83-3.82	0.1909
No	14	28	42				14	40	54			
Total	90	147	237				97	188	285			
Days in plots (< 3 months)												
Yes	75	116	191	1.98	0.79-4.94	0.2015	77	137	214	1.66	0.82-3.37	0.2209
No	15	31	46				20	51	71			
Total	90	147	237				97	188	285			
Times slept at plot												
Yes	33	45	78	1.28	0.71-2.31	0.4968	22	26	48	2.28	1.09-4.75	0.0337
No	57	102	159				75	162	237			
Total	90	147	237				97	188	285			
Number of plots on creeks												
Yes	35	49	84	1.25	0.67-2.31	0.5723	35	52	87	1.56	0.88-2.75	0.1612
No	55	98	153				62	136	198			
Total	90	147	237				97	188	285			
Days in creeks (< 3 months)												
Yes	30	39	69	1.43	0.76-2.71	0.3403	29	41	70	1.62	0.88-2.95	0.1543
No	60	108	168				68	147	215			
Total	90	147	237				97	188	285			
Number of plots on slopes												
Yes	67	111	178	1.11	0.52-2.36	0.9469	71	127	198	1.39	0.75-2.56	0.3678
No	23	36	59				26	61	87			
Total	90	147	237				97	188	285			
Days in slopes (< 3 months)												
Yes	64	107	171	1.05	0.51-2.14	0.9503	65	119	184	1.23	0.68-2.24	0.5999
No	26	40	66				32	69	101			
Total	90	147	237				97	188	285			
Number of plots elsewhere												
Yes	5	10	15	0.79	0.24-2.60	0.9226	6	13	19	0.91	0.35-2.35	0.9675
No	85	137	222				91	175	266			
Total	90	147	237				97	188	285			
Days in elsewhere (< 3 months)												
No	86	139	225	1.14	0.33-4.01	0.9195	91	175	266	1.10	0.42-2.86	0.9675
Yes	4	8	12				6	13	19			
	90	147	237				97	188	285			

Table D.IV.2. Comparison of Human Outdoor Behaviour by Age Group

Exposure	Children						Adults					
	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value	Case	Control	N	Matched Odds Ratio	Confidence Limits	P-value
Number of plots												
Yes	131	228	359	1.64	0.91-2.95	0.1267	28	39	67	NA		
No	26	63	89				2	5	7			
Total	157	291	448				30	44	74			
Days in plots (< 3 months)												
Yes	125	216	341	1.70	0.96-3.01	0.0912	27	37	64	2.50	0.21-30.29	0.8119
No	32	75	107				3	7	10			
Total	157	291	448				30	44	74			
Times slept at plot												
Yes	42	61	103	1.39	0.83-2.33	0.2442	13	10	23	2.13	0.76-6.01	0.2141
No	115	230	345				17	34	51			
Total	157	291	448				30	44	74			
Number of plots on creeks												
Yes	57	76	133	1.53	0.97-2.41	0.0794	13	25	38	0.49	0.15-1.64	0.3463
No	100	215	315				17	19	36			
Total	157	291	448				30	44	74			
Days in creeks (< 3 months)												
Yes	48	59	107	1.79	1.09-2.93	0.0265	11	21	32	0.75	0.27-2.09	0.7639
No	109	232	341				19	23	42			
Total	157	291	448				30	44	74			
Number of plots on slopes												
Yes	110	208	318	1.02	0.62-1.67	0.9663	28	30	58	NA		
No	47	83	130				2	14	16			
Total	157	291	448				30	44	74			
Days in slopes (< 3 months)												
Yes	102	197	299	0.95	0.59-1.53	0.9177	27	29	56	NA		
No	55	94	149				3	15	18			
Total	157	291	448				30	44	74			
Number of plots elsewhere												
Yes	11	20	31	1.01	0.47-2.20	0.8677	0	3	3	NA		
No	146	271	417				30	41	71			
Total	157	291	448				30	44	74			
Days in elsewhere (< 3 months)												
No	147	273	420	0.93	0.42-2.06	0.9729	30	41	71	NA		
Yes	10	18	28				0	3	3			
	157	291	448				30	44	74			

Table B.IV.1 . Summary of Matched Analysis +
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Factors	Matched Odds Ratio		
	Pooled	Region 1	Region 2
	No. (95% Conf. limits)	No. (95% Conf. limits)	No. (95% Conf. limits)
I. House characteristics			
Wall material: Stone	2.64 (1.27-5.48) **	2.51 (1.22-5.29) *	NA
Windows in the house	1.25 (0.75-2.10)	0.73 (0.38-1.41)	2.91 (1.10-7.69) *
House windows open	1.40 (0.95-2.08)	0.88 (0.46-1.69)	1.86 (1.11-3.11) *
Holes in bedroom windows	2.23 (1.12-4.45) *	6.33 (0.75-53.6)	1.68 (0.78-3.62)
Chimney	1.99 (1.19-3.34) *	1.85 (0.90-3.79)	2.03 (0.96-4.29)
Age of the house	1.76 (1.15-2.70) *	1.20 (0.60-2.38)	2.45 (1.39-4.33) **
Bedroom size	1.47 (1.00-2.15) *	1.31 (0.75-2.29)	1.53 (0.91-2.59)
II. Findings around the house			
Distance to creeks < 100 m	1.83 (1.10-3.03) *	3.19 (1.22-2.36) *	1.52 (0.81-2.85)
Distance to river > 30 m	2.81 (1.37-5.76) **	0.90 (0.19-4.24)	4.59 (1.87-11.2) **
Distance to road > 30 m	1.88 (1.24-2.86) **	2.64 (1.27-5.48) *	1.61 (0.95-2.72)
Distance to waterways	1.74 (1.14-2.68) *	0.92 (0.47-1.81)	2.82 (1.57-5.07) **
Neighbouring kitchen garden	1.43 (0.91-2.25)	1.02 (0.57-1.84)	2.36 (1.14-4.86) *
III. Human indoors behaviour			
House modification	1.89 (1.15-3.09) *	1.74 (0.78-3.85)	1.89 (1.00-3.58)
Home-made kerosene lamp	1.17 (0.75-1.84)	2.88 (1.16-7.16) *	0.84 (0.49-1.43)
Proprietary Kerosene lamp	1.44 (0.96-2.18)	3.50 (1.48-8.29) **	1.03 (0.63-1.66)
Stored Wood	2.88 (1.18-7.06) *	4.83 (1.24-18.8) *	1.55 (0.43-5.58)
IV. Human outdoors behaviour			
Slept in plots	1.33 (0.88-2.01)	1.28 (0.71-2.30)	2.28 (1.09-4.71) *
Days in creeks	1.49 (0.97-2.31)	1.43 (0.76-2.70)	1.62 (0.88-2.93)
Irrigation work at night	2.96 (1.37-6.36) **	3.73 (1.27-10.3) *	2.25 (0.74-6.80)

* $p < 0.05$ ** $p < 0.01$
+ level of significance $p < 0.05$

Figure 9. Frequency of Selected House Characteristics in Controls in Regions 1 and 2, Peru 1991–1992

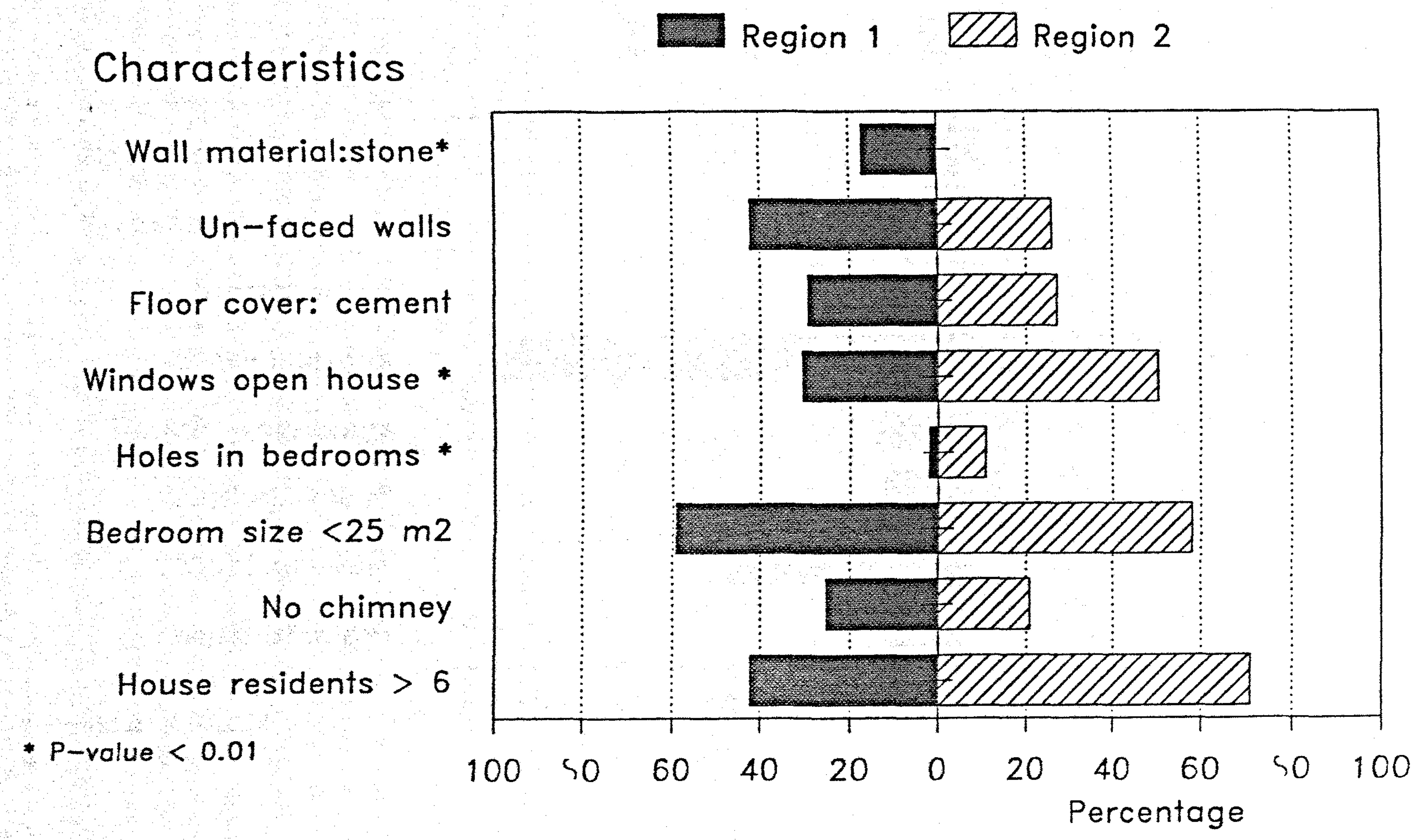


Figure 10. Frequency of Human Behaviour
Indoor and Outdoor in Controls in
Regions 1 and 2, Peru 1991–1992

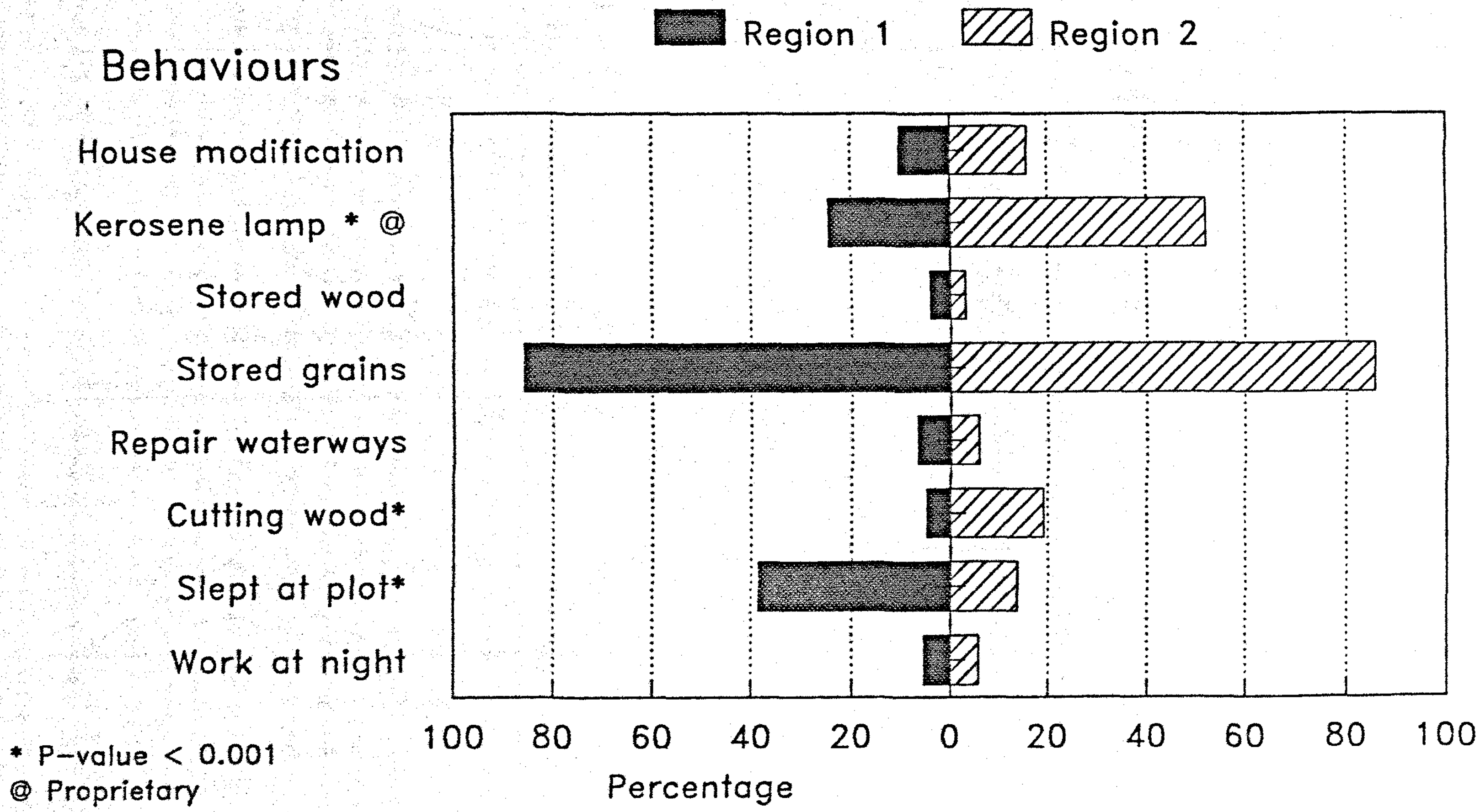
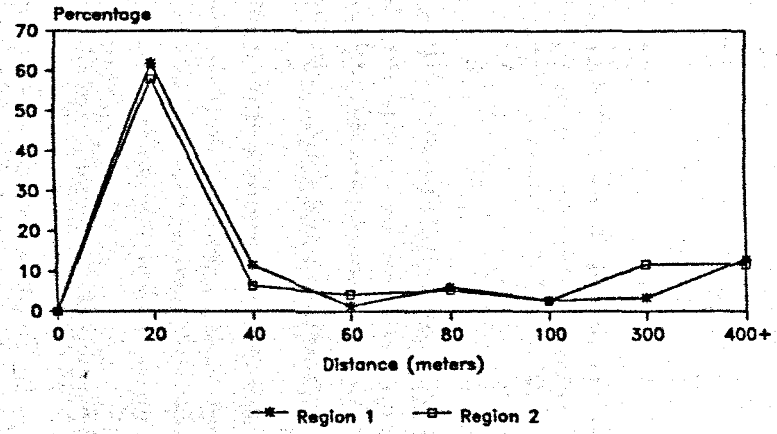
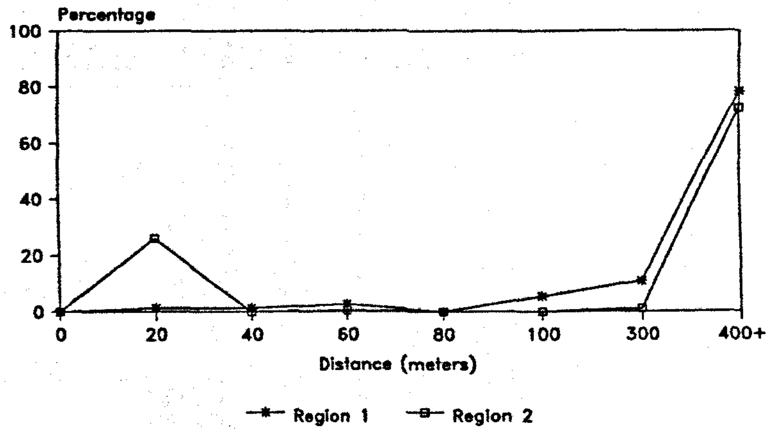


Figure 11. Frequency of Distance from House to Road in Controls in Regions 1 and 2.



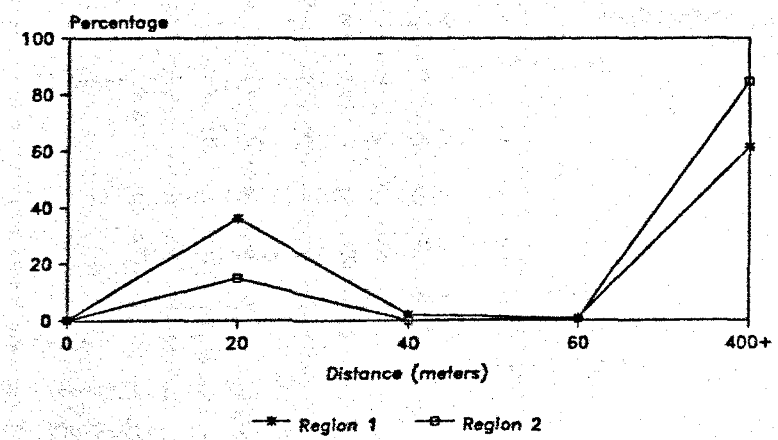
$p > 0.05$

Figure 12. Frequency of Distance from House to River in Controls in Regions 1 and 2.



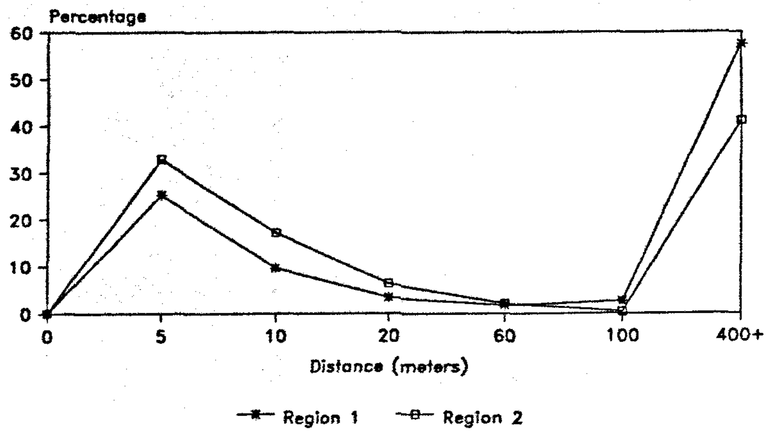
$p < 0.001$

Figure 13. Frequency of Distance from *House to Neighbouring Kitchen Gardens* in Controls in Regions 1 and 2.



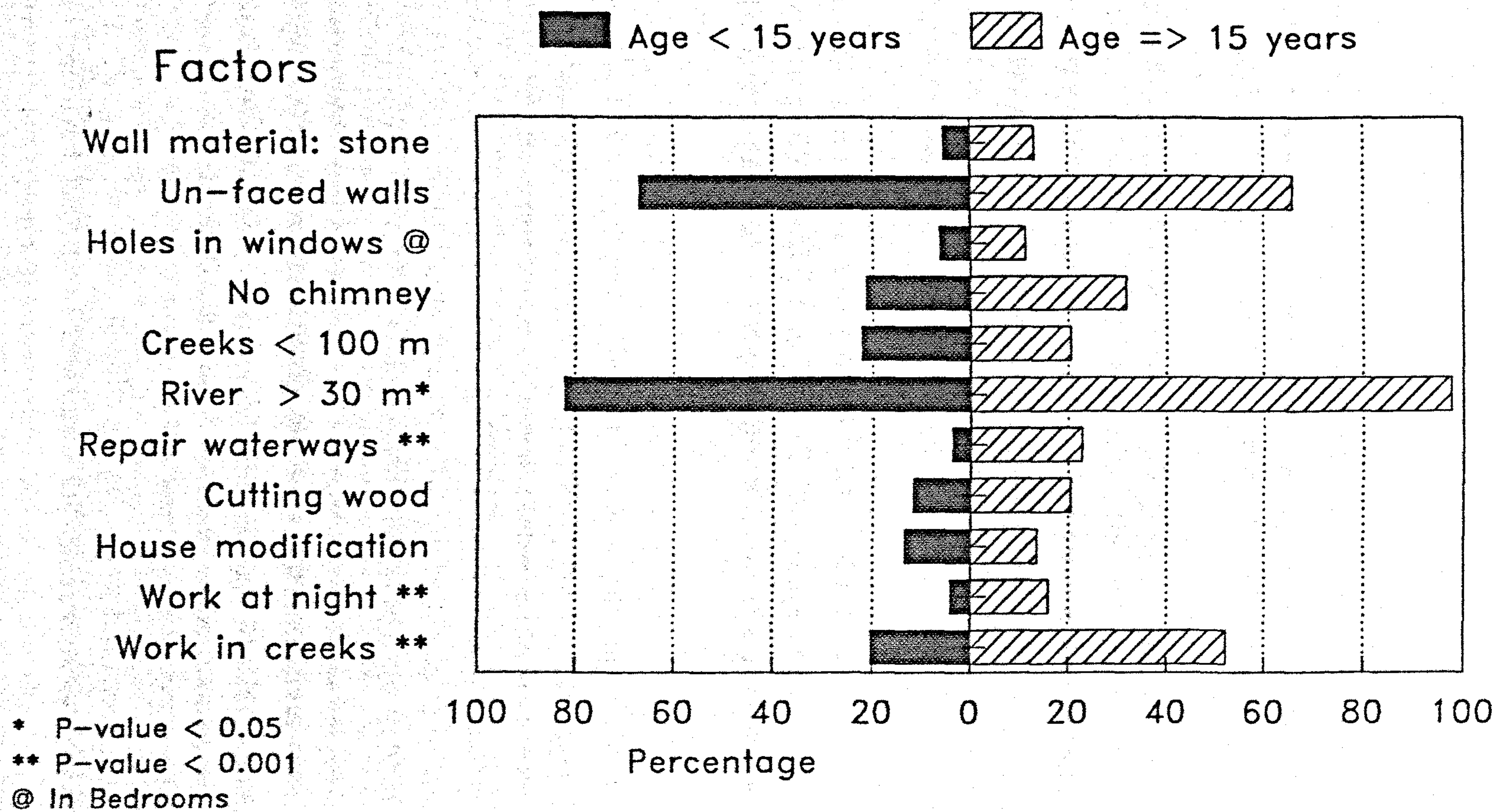
$p < 0.001$

Figure 14. Distance From House to *Kitchen Gardens in Controls in* Regions 1 and 2.



$p = 0.02$

Figure 15. Frequency of Selected Factor
in Controls in Regions 1 and 2
Case–Control Study, Peru 1991–1992



C. MULTIVARIATE ANALYSIS

The variables chosen from the matched analysis were analyzed using a conditional logistic regression model appropriate for pair-matched data (Breslow & Day 1980, Schlesselman 1982). Every potential risk factor was represented in the model with a single categorical variable (Table E.I.1).

Tables E.I.1 to E.III.2 present the results of the multivariate analysis. The Tables for each model describe the variable name, the estimated logistic regression coefficient ß with its standard error, p-value and odds ratio with 95% confidence bounds. The overall deviance is at the bottom of each table. Regression coefficients represent the log odds ratio for a unit of change in a variable adjusted by maximum likelihood.

Three models for the pooled data (Tables E.I.1 to E.I.3) and two for each region are presented (Tables E.II.1 to E.III.2). They represent the best models choosen by comparison of the log of the ratio of the maximized likelihood estimates.

Model 1 examined the hypothesis that logit risk of uta in all study regions is a linear function of candidate variables (Table E.I.1). The model was extended adding, firstly, interactions by region (Table E.I.2) and later age (Table E.I.3). Holes in bedroom windows (p= 0.015), no chimney inside the house (p= 0.034), distance of roads from the house (> 30 meters; p= 0.007), stored wood in house (p= 0.025) and repairing waterways (p= 0.032) were risk factors associated with transmission of uta and stored grains was a protective factor (p= 0.039). Five statistically significant interactions were detected, one of them with region 2 (Piura) and four by age, but for all of them OR's were close to one (Table E.I.3). These variables were: floor cover, kitchen gardens, proprietary kerosene lamps, cows with age (children) and rivers with region 2. The results of the likelihood ratio tests indicated that the fit of model was improved, both by adding terms for interaction by region and by age group (Tables E.I.1 to E.I.3).

Model 2 examined the same hypothesis as model 1, but for Lima plus Ancash only (Table E.II.1), to allow for testing of interactions by age (Table

Table E.I.0. Conventions Used in Variables Included in Multivariate Analysis .

NPISO	Number of floors (0: 1 vs. 1: 2 or more)
FLOOR	Cover floor (0: cement & others vs. 1: earth)
WALL	Wall material (0: adobe vs. 1: stone)
COVEW	Cover wall (0: no vs. 1: yes)
NTOVN	Number of windows (0: 0 vs. 1: 1+)
NVENA	House window open (0: close vs. 1: open)
HOLES	Holes in bedroom windows (0: no vs. 1: yes)
WDHS	Holes in house windows (0: no vs. 1: yes)
EDCA	Age of the house (0: < 7 years vs. => 7 years)
TADOR	Bedroom size (0: => 25 sqm vs. 1: < 25 sqm)
ORIHU	Chimney inside the house (0: no vs. 1: yes)
DISCO	Kitchen distance (0: < 4 m vs. 1: > 4 m)
CREEK	Distance to creek (0: > 100 m vs. 1: =< 100 m)
ROAD	Distance to road (0: =< 30 m vs. 1: > 30 m)
RIVER	Distance to river (0: > 30 m vs. 1: =< 30 m)
CHANL	Distance to waterways (0: => 200 m vs. 1: < 200)
VECIT	Neighbouring kitchen garden (0: no vs 1: yes)
GARD	Kitchen garden (0: no vs. 1: yes)
NRESI	Number of residents (0: < 6 vs. => 6 persons)
MODIC	Modifications of the house (0: no vs. 1: yes)
KERO	Proprietary Kerosene lamp (0: no vs. 1: yes)
MECHE	Home-made Kerosene lamp (0: no vs. 1: yes)
FRUIT	Stored fruit indoors (0: no vs. 1: yes)
WOOD	Stored wood indoors (0: no vs. 1: yes)
GRAIN	Stored grains indoors (0: no vs. 1: yes)
COW	Cows around dwellings (0: no vs. 1: yes)
GOAT	Goats around dwellings (0: no vs. 1: yes)
SHEEP	Sheep around dwellings (0: no vs. 1: yes)
CHICK	Chickens around dwellings (0: no vs. 1: yes)
CATS	Cats indoors (0: no vs. 1: yes)
DOGS	Dogs around dwellings (0: no vs. 1: yes)
NVCAN	Repairing waterways (0: no vs. 1: yes)
DESMT	Weeding (0: no vs. 1: yes)
TALA	Cutting wood (0: no vs. 1: yes)
NVREG	Irrigation work at night (0: no vs. 1: yes)
PLOTS	Number of plots (0: 1 vs. 1: 2+)
NDAY	Days in plots (0: no vs. 1: yes)
NUCHA	Slept at plots (0: no vs. 1: yes)
NNCQ	Plots in creeks (0: no vs. 1: yes)
NDIAQ	Days in creeks (0: no vs. 1: yes)
NDIAL	Days in slopes (0: no vs. 1: yes)
REGIO	Study region (1: Lima+Ancash vs. 2: Piura)
AGEGP	Age group (0: < 15 years vs. 1: => 15 years)

Table E.I.1 . Risk Factors Associated with the Transmission of Uta in Pool Data (Model 1) Case-Control Study o Study on Cutaneous Leishmaniasis, Peru 1991-1992

Factors	Coefficient	Standard Error	P-value	Odds Ratio	95% Confidence Bounds
Distance to road > 30 m	0.63	0.23	0.01	1.87	1.18 - 2.96
Chimney	0.59	0.29	0.04	1.80	1.06 - 3.15
Distance to river > 30 m	-0.99	0.40	0.01	0.37	0.17 - 0.81
Distance to creek < 100 m	0.62	0.28	0.03	1.85	1.07 - 3.20
Holes in bedroom windows	0.89	0.39	0.02	2.43	1.13 - 5.20
Stored wood	1.19	0.49	0.02	3.27	1.26 - 8.52
Stored grains	-0.56	0.26	0.03	0.57	0.34 - 0.96
Repairing waterways	0.73	0.37	0.05	2.07	1.01 - 4.27

Deviance = 329.87

Likelihood Ratio Statistic on 1 DF = 3.95, p = 0.047

Table E.I.2. Fit of the Model Adding Interactions by Region

Factors	Coefficient	Standard Error	P-value	Odds Ratio	95% Confidence Bounds
Distance to road > 30 m	0.66	0.24	0.01	1.93	1.21 - 3.07
Chimney	0.60	0.29	0.04	1.82	1.04 - 3.19
Distance to river > 30 m	2.75	1.78	0.12	15.70	0.48 - 514.4
Distance to creek < 100 m	0.65	0.29	0.02	1.92	1.10 - 3.36
Holes in bedroom windows	0.85	0.40	0.04	2.33	1.06 - 5.13
Stored wood	0.85	0.49	0.02	3.23	1.27 - 8.43
Stored grains	1.17	0.26	0.04	0.58	0.35 - 0.98
Repairing waterways	0.73	0.37	0.05	2.07	0.99 - 4.28
Region.river	-2.06	0.98	0.04	0.13	0.02 - 0.87

Deviance = 325.72

Likelihood Ratio Statistic on 1 DF = 4.15, p = 0.042

Table E.I.3. Fit of the Model Adding Interactions by Age

Factors	Coefficient	Standard Error	P-value	Odds Ratio	Bounds
Distance to road > 30 m	0.66	0.24	0.01	1.97	1.22 - 3.32
Chimney	0.60	0.29	0.04	1.90	1.05 - 3.44
Distance to river > 30 m	1.94	2.06	0.35	6.92	0.12 - 395.4
Distance to creek < 100 m	0.54	0.31	0.08	1.71	0.94 - 3.12
Holes in bedroom windows	0.85	0.39	0.02	2.81	1.28 - 7.29
Stored wood	0.85	0.49	0.02	3.15	1.11 - 8.34
Stored grains	1.17	0.26	0.03	0.57	0.34 - 0.98
Repairing waterways	0.73	0.37	0.05	2.37	1.03 - 5.17
Region	-1.09	1.36	0.42	0.33	0.02 - 4.76
Region.river	-1.63	1.12	0.15	0.20	0.02 - 1.75
Age	-0.05	0.05	0.32	0.95	0.85 - 1.05
Age.floor	0.06	0.03	0.07	1.06	0.99 - 1.13
Age.gard	-0.04	0.03	0.14	0.96	0.90 - 1.15
Age.kero	0.06	0.03	0.02	1.06	1.00 - 1.11
Age.cow	0.01	0.01	0.50	1.01	0.99 - 1.02
Floor	-0.00	0.38	0.99	1.00	0.48 - 2.10
Gard	-0.22	0.37	0.56	0.80	0.39 - 1.67
Kero	0.04	0.36	0.91	0.96	0.47 - 1.94
Cow	0.09	0.10	0.32	1.10	0.91 - 1.32

Deviance = 303.72

Likelihood Ratio Statistic on 6 DF = 2.83, p = 0.83

Table E.II.1. Risk Factors Associated with the Transmission of Uta in Region 1 (Model 2) Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Factors	Coefficient	Standard Error	P-value	Odds Ratio	95% Confidence Bounds
Proprietary kerosene lamp	1.89	0.56	< 0.001	6.61	2.21 - 19.75
Number of residents > 6	1.45	0.42	< 0.001	4.26	1.87 - 9.70
Wall material: stone	1.08	0.30	< 0.001	2.95	1.65 - 5.25
Cutting wood	1.99	0.65	0.00	7.33	2.04 - 26.36
Chimney	1.59	0.48	< 0.001	4.89	1.91 - 12.50
Distance to road > 30 m	1.36	0.52	0.01	3.88	1.41 - 10.74
Kitchen garden	-1.04	0.47	0.03	0.35	0.14 - 0.88

Deviance = 114.83

Likelihood Ratio Statistic on 1 DF = 5.47, p = 0.019

Table E.II.2. Fit of the Model Adding Interactions by Age

Factors	Coefficient	Standard Error	P-value	Odds Ratio	95% Confidence Bounds
Proprietary kerosene lamp	1.89	0.56	< 0.001	6.61	2.21 - 19.75
Number of residents > 6	1.45	0.42	< 0.001	4.26	1.87 - 9.70
Wall material: stone	1.08	0.30	< 0.001	2.95	1.65 - 5.25
Cutting wood	1.99	0.65	0.00	7.33	2.04 - 26.36
Chimney	1.59	0.48	< 0.001	4.89	1.91 - 12.50
Distance to road > 30 m	1.36	0.52	0.01	3.88	1.41 - 10.74
Kitchen garden	-1.04	0.47	0.03	0.35	0.14 - 0.88

Deviance = 114.83

Likelihood Ratio Statistic on 1 DF = 5.47, p = 0.019

E.II.2). The significant associations were: walls built of stone ($p < 0.001$), no chimney inside the house ($p < 0.001$), distance of roads from the house (> 30 meters; p= 0.009), no kitchen garden ($p = 0.026$), more than 6 residents per house ($p < 0.001$), the use of kerosene lamps without a glass tube ($p < 0.001$), and cutting wood ($p = 0.002$). The results of likelihood ratio tests indicated that the fit of the model was not improved when the terms for interactions by age group were added (Table E.II.2).

Model 3 examined the same hypothesis as model 1, but for Piura region (Tables E.III.1 and E.III.2). The significant associations were: no floor cover ($p = 0.024$), distance from river < 30 meters ($p = 0.011$), the existence of neighbouring kitchen gardens ($p = 0.013$), having cows around dwellings ($p = 0.011$), and irrigation work at night ($p = 0.011$). As for region 1, above, the likelihood ratio tests indicated that the fit of the model was not changed when terms for interactions by age group were added (Table E.III.2).

A further two models comparing children and adults were tested in order to verify the interactions by age group. No significant results were observed.

The essential results of multivariate analysis are summarized in Table E.IV.1.

D. POPULATION ATTRIBUTABLE RISK

In order to estimate the proportion of the disease that could be explained by a set of the more significant factors detected, and to evaluate the potential impact of an intervention program, those factors significant in MVA were used to calculate the PAR. Table F.I.1 shows the PAR and ORs (estimated from MVA) for three factors associated with indoor transmission in region 1. Notice that the summary PAR is not the result of adding PAR's for constituent factors; it is the adjusted population attributable risk for all separate factors (Bruzzi *et al.* 1985).

Appendix 6 shows the detailed distribution of cases and their matched controls in each stratum obtained by cross-classifying the three risk factors,

Table E.III.1. Risk Factors Associated with the Transmission of Uta in Region 2 (Model 3) Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Factors	Coefficient	Standard Error	P-value	Odds Ratio	95% Confidence Bounds
Distance to river < 30 m	-1.19	0.47	0.01	0.30	0.12 - 0.76
Cows around dwellings	0.26	0.10	0.01	1.30	1.06 - 1.58
Neighbouring kitchen garden	1.08	0.43	0.01	2.94	1.26 - 6.86
Irrigation work at night	0.81	0.32	0.01	2.25	1.20 - 4.19
Uncover floor	0.82	0.36	0.02	2.27	1.11 - 4.63

Deviance = 166.92

Likelihood Ratio Statistic on 1 DF = 5.47, p = 0.019

Table E.III.2. Fit of the Model Adding Interactions by Age

Factors	Coefficient	Standard Error	P-value	Odds Ratio	95% Confidence Bounds
Distance to river < 30 m	-1.19	0.47	0.01	0.30	0.12 - 0.76
Cows around dwellings	0.26	0.10	0.01	1.30	1.06 - 1.58
Neighbouring kitchen garden	1.08	0.43	0.01	2.94	1.26 - 6.86
Irrigation work at night	0.81	0.32	0.01	2.25	1.20 - 4.19
Uncover floor	0.82	0.36	0.02	2.27	1.11 - 4.63

Deviance = 166.92

Likelihood Ratio Statistic on 1 DF = 5.47, p = 0.019

Table E.IV.1 . Summary of Multivariate Analysis
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

Factors	Odds Ratio		
	Pooled No. (95% Conf. limits)	Region 1 No. (95% Conf. limits)	Region 2 No. (95% Conf. limits)
I. House characteristics			
Wall material: Stone		2.95 (1.65- 5.25)**	
Uncover floor			2.27 (1.11-4.68)*
Holes in bedroom windows	2.81 (1.22-6.48)*		
Chimney	1.90 (1.05-3.44)*	4.89 (1.91-12.50)**	
II. Findings around the house			
Distance to river > 30 m			3.28 (3.09-8.45)*
Distance to road > 30 m	1.97 (1.21-3.21)*	3.88 (1.41-10.74)**	
No kitchen garden		2.83 (1.15- 4.15)*	
Neighbouring kitchen garden			2.94 (1.26-6.86)*
III. Human indoors behaviour			
Number of residents > 6		4.25 (1.87- 9.70)**	
Stored Wood	3.15 (1.16-8.58)*		
No stored grains	1.77 (1.40-2.65)*		
Proprietary Kerosene lamp		6.61 (2.21-19.75)**	
Cows around dwelling			1.30 (1.06-1.58)*
IV. Human outdoors behaviour			
Repair waterways	2.37 (1.08-5.23)*		
Cutting wood		7.38 (2.08-26.36)*	
Irrigation work at night			2.25 (1.20-4.19)*

* $p < 0.05$ ** $p < 0.001$

Table F.I.1. Relative Risk and Population Attributable Risk for Three Factors Associated with Transmission Inside Houses in region 1 : Kerosene Lamp, Having a Chimney and Living in a Stone House.

Factors	Code Model	RR Adjusted for the other factors	Population Attributable Risk
Wall material			
Adobe	0		
Stone	1	2.95	0.202
Chimney			
Yes	1	4.89	0.402
No	0		
Kerosene lamp			
Others	0		
Proprietary	1	6.61	0.38
Summary PAR (all three factors)			0.792

the distribution of the adjusted factors in the population without disease (number of controls in each strata/total number of controls), and the distribution of adjusted factors in population with uta (number of cases in each strata/total number of cases). Odds ratios were calculated when strata contained feasible information.

CHAPTER IV: DISCUSSION AND IMPLICATIONS OF THE FINDINGS

In regions 1 and 2 we have identified risk factors which imply that transmission occurs (a) inside houses, (b) outside but close to houses, (c) close to houses, but not clearly indoors or outdoors, and (d) away from houses.

In region 1 we found three risk factors of type a (using a kerosene lamp, having a chimney and living in a stone house), one of type b (cutting wood), and three of type c (living in a house > 30 m from road, with a vegetable garden and living in a house > 6 persons). In region 2, we found four risk factors of type c (living in a house having an unfinished floor, with cows and a neighbouring vegetable garden nearby, and living > 30 m from a river), and one of type d (doing irrigation work at night).

Before offering possible explanations for these results, we consider some methodological constraints. Because bias and/or a precision error could be introduced, objections can be raised at different levels.

A. Methodological Considerations

A. 1. Design

Our study has been a population-based case-control study, where the population was defined geographically and temporally (primary base using the terminology of Miettinen 1985), with complete case identification. The inhabitants of the study area became study cases only when they developed disease during the period of investigation. An advantage of concurrent design is that a subject chosen to be a control for a case is not excluded from the set of controls because of subsequent development of disease. Thus, the 11 controls who subsequently developed uta in our study also served as cases. Further, control selections at the various times of diagnosis of uta cases were mutually independent and not influenced by their use as controls for other uta cases (Lubin *et al.* 1984, Rodrigues & Kirwood 1990).

In this study we excluded patients with recurrent lesions, because recurrent lesions could be the consequence of two different mechanisms, reactivation of a persistent infection or exogenous reinfection, and each has different implications (Saravia *et al.* 1990).

A disadvantage that has been reported in matched studies is the exclusion of cases when no matched controls can be found (MacMahon & Plug 1970, Thompson *et al.* 1982, Wacholder *et al.* 1992c). In this study, only 3.9% cases were excluded for this reason.

A.2. Sampling

The sample size in the original proposal was calculated using a non-matched design (Cousens et al. 1988). This sample was later re-calculated for a pair-matched study using the formulae of Schlesselman (1982, p.161), with assumptions otherwise the same. The estimate was 186 matched pairs, very similar to the sample size calculated for the unmatched design.

High and different migration rates among cases and controls could introduce bias. When people emigrate from Andean communities they usually go to coastal cities for economic, social and political reasons (Martinez 1987). Two types of migration occur, permanent in young workers and temporary among older people (Aramburu 1983, Martinez 1987). The former is more common in the areas where we carried out our studies. There was a low rate of emigration (probably less than 5%) during the two years of this study in all regions (C.R. Davies, unpublished information). Internal migration was very low because the work in these places is family based. We have no evidence to suggest selective emigration during the study. As far as we know, no patient was treated out of the area. All patients received free treatment in their own villages (health posts or performed by health promoters). The cost of the same treatment in cities is around $US

140 plus travel and hotel expenses. This is unaffordable for the majority of patients from rural areas.

Bias by inaccessibility (persons of the base not followed because they lived in places with low accessibility) was limited because special effort was made to evaluate them.

Another potential source of bias is an incomplete ascertainment of cases. This can sometimes could be problematic in a primary base when detection is difficult (Savitz *et al.* 1988). Uta cases cannot always be diagnosed, especially in the earlier stages (less than one month) when clinical characteristics are still undefined and/or MST is negative (Pessôa & Barreto 1948, Cuba *et al.* 1984). However, the close follow-up of the population by health promoters and field workers of our team (every 3 months) made the chance of wrongly screening controls slight. All suspected cases were closely observed and usually their status was resolved within one month.

Bias by refusal upsets ascertainment of both cases and controls. Refusals included rejection of diagnostic procedures, denying the existence of scars, or not collaborating with questionnaires. The latter was not observed, and only two persons without disease (0.3%) refused MST. An expert clinician usually re-examined blind all problem cases selected by the supervisor. The criteria were: persons with non-characteristic scars possibly due to uta, persons MST positive who denied having had a lesion, persons MST positive and scar negative, or MST negative and scar positive. Approximately 10% of the controls were re-checked for these reasons and the information was corrected when necessary.

We estimate that the magnitude of the bias introduced by case and control selection was low in this study.

A.3. Comparable Accuracy of Cases and Controls

Failure to diagnose cases and/or to measure candidate risk factors accurately could introduce bias or precision errors. Misclassification could introduce bias by considering as cases people who are controls or vice versa. The diagnosis of cutaneous leishmaniasis is based on a combination of both clinical history and characteristics of the lesion, plus immunological and/or parasitological tests (Llanos-Cuentas *et al.* 1984, Weigle *et al.* 1987, Navin *et al.* 1990). In our experience the clinical diagnosis of uta is not difficult in the majority of endemic areas. Because uta is generally a disease of children, differential diagnosis due to chronic skin lesions is infrequent. The more important diagnostic problems were staphylococcal or streptococcal cutaneous infections. These were specially common in the warm areas such as Piura, and during the rainy season. Antibacterial therapy for a period of 4-7 days normally resolved problems of this kind. All non-characteristic lesions were evaluated for other possible aetiologies, but diseases such as sporothrycosis, other subcutaneous mycoses or tuberculosis were not detected during the study period. Because, pentavalent antimonials are not available at the health posts, and because they are expensive, we rarely found patients who had previous specific therapy that might have modified their lesions.

The correlation between MST and scarred uta is high (Llanos-Cuentas & Davies 1992, Davies *et al.* submitted) in the whole population and higher still in persons under 20 years (Llanos-Cuentas & Davies 1992, pp.294-296). Chagas' disease or visceral leishmaniasis were not a source of cross-reactivity because they not have been described in these areas. Thus, the diagnosis of susceptible people was not a problem. On the other hand, 10 of 11 controls that became cases developed the disease after six months; only one control developed a lesion after four months, and there is a small chance that he was infected when selected as a control. The mean incubation period of uta calculated in endemic areas was around one month (Llanos-Cuentas & Davies 1992), estimated by cross-correlations between monthly sandfly densities and monthly incidence rates.

Recall and interviewer bias can lead to either over- or underestimation of the association between exposure and disease (Hennekens & Buring 1987, Hulley & Cummings 1988). Differential errors can be hard to avoid in case-control studies in which exposure information is obtained from interviews with the subjects. Individuals (i.e. parents) who have experienced the disease are usually ready answer questions about possible "causes" of the illness. Behavioural questions are particularly vulnerable to this kind of bias, e.g. the times spent on outdoor activities. In order to minimize bias, only one interviewer completed a questionnaire for a suspected case and control pair. This objection would have been important only if the variance of cases and controls showed significant differences, but this was not observed (Tables A.III.2 to A.IV.2). Nevertheless, during the analysis these factors were managed as bivariate categories (presence or absent). Our impression is that the biases introduced by these problems were similar for cases and controls.

A.4. Confounders

One of the major challenges of non-experimental epidemiology is the control of confounding factors because they distort (in part or totally) the estimation of the effect (Rothman 1986, Hennekens and Buring 1987). Matching is one of the methods used to control confounding in analytic epidemiological studies whose primary objective is the elimination of biased comparisons between cases and controls (Schlesselman 1982, Miettinen 1985). But a matched design must be accompanied by a matched analysis (Schlesselman 1982).

We carried out a case-control study matched by age, sex and place of residence. Age, sex and race are often used as matching variables because they are usually strong confounders and because their effects are usually well known from descriptive epidemiology (MacMahon & Plug 1970). The analysis of the epidemiological information of Purisima area between October 1986 to March 1989 (Llanos-Cuentas, unpublished information) showed that the incidence rate in unscarred individuals under 15 years was 5.6 times higher than in those over this age. At the same time, the incidence risk in females under 15 years was 1.4 times higher than males of the same age group. Thus, there are good reasons to match by age and sex.

Matching by place of residence is a more controversial point. Sometimes in case-control studies, controls are selected from family members or neighbours (Butraporn *et al.* 1986, Clemens *et al.* 1988). In the two published case-control studies of leishmaniasis which have an adequate design, matching was by town ('vereda' in Colombia, Weigle *et al.* 1992) and by nearest neighbour (Rojas-Ocampo, 1993). We made the following relevant observations in our areas: (i) in Purísima valley, incidence varies strongly with altitude (Villaseca *et al.* in press), (ii) Herrer (1951, 1957) suggested there is great variation between valleys as well, and more recent data have supported Herrer's suggestion (Llanos-Cuentas & Davies 1992), (iii) the variation in transmission rate is closely correlated with both spatial and temporal distribution of the potential vector (Villaseca *et al.* in press, Davies *et al.* in press). We therefore decided to match by village. There is however the possibility that matching by village disallows the investigation of some important risk factors. Suppose that having a dog is a risk factor for uta, but that risk depends on the number of dogs per village, rather than the number per house. The real association between dogs and disease would be obscured by matching cases and controls from the same village.

Our OR's were moderate, but in a multifactorial disease such as leishmaniasis, where host, vectors, reservoirs, ecology and geographic variables play a role in the maintenance of endemicity around human settlements for a long time (Neronov & Gunin 1971), we do not expect to find risk factors with higher odds ratios. In this respect, our results are consistent with those reported by Rojas-Ocampo (1993) in Costa Rica.

The extent of bias from unmeasurable or uncontrolled confounders depends on the strengths of their associations with study exposures and disease risk (Breslow & Day 1980, Schlesseman 1982), but no other important confounders were detected in this study.

A.5. Analysis

Errors could be introduced in the analyses because of inadequate or incomplete selection of variables in models. Failure to include critical variables obviously would lead to the wrong functional relationships.

The goal is to yield the best possible model with the constraints of the available data. Criteria for including variables in a model may vary from one discipline to another or among the epidemiologists. When we used the traditional $p < 0.05$ as the screening criterion for selection of candidate variables the model for region 1 was 'unstable' i.e. the importance of risk factors varied with their order of inclusion in the models. Later, we verified that the screening criteria $p < 0.05$ failed to identify risk factors by both linear regression (Bendel & Afifi 1977) and logistic regression (Mickey & Greenland 1989). One advantage of including a larger number of variables is a better control of potential confounders. A disadvantage is that the model incorporates some variables of questionable importance. The criterion $p < 0.25$ that we finally used (Hosmer & Lemenshow 1989) apparently was adequate. All variables with biological plausibility in our study were below this level.

Logistic regression with the pooled data include five possible interactions (Table E.I.3), one between regions and four with age, but all had OR's close to unity with small confidence intervals (e.g. interaction children and kitchen gardens has OR=1.05 with c.i.: 1.008-1.096). These interactions therefore have a negligible effect on the risk of disease and are not discussed further.

A.6. Limitations of Case-Control Study

Case-control studies, like any other methodology, have their limitations. We should be especially cautious with case-control design as a new methodology for the study of highly endemic diseases (Rodrigues & Kirkwood 1990). In leishmaniasis the limitations are both technical and practical. The design requires an adequate epidemiological background, experience in field work, and good relation with the communities in order to obtain reliable information. The other important limitation is the analysis which demands skills in advanced statistical methods (matched analysis, multivariate analysis, attributable risk). The cost of case-control study is less expensive than long term longitudinal studies, but this was not a very cheap study. The cost was at least three times more that the economic support received from TDR/WHO. This study was only possible because other epidemiological studies were being carried out simultaneously in the same areas.

B. Risk Factors and Hypothetical Explanations.

Our data show that approximately half of the variables selected by matched analysis or MVA differed between regions (Tables B.V.1 and E.IV.1). This could be explained by variation in the frequency of exposure to variables between regions, or by variation in the magnitude of their effects. Stone walls are not a risk factor in region 2 because in that region no houses are built of stone (Figure 9, Table C.I.1). Similarly, risk factors such as rivers (Figure 12, Table C.II.1), kitchen gardens and neighbouring kitchen gardens (Figures 13 & 14, Table C.II.1) can be explained by the fact that they are more frequent in region 2 than in region 1. However, some variables with high frequency in region 2, such as the use of kerosene lamps and cutting wood (Figure 10), were risk factors in region 1 only. Thus, the frequency of exposure can not explain all the differences. Earth floors (Figure 9, Table C.I.1), chimneys (Figure 9, Table C.I.1), stored wood or grains (Figure 10, Table C.III.1), irrigation work at night (Figure 10, Table C.IV.1), and distance from road to house (Figure 11, Table C.II.1) had similar effects in both regions but were significant only in one region.

Possible explanations for each risk factor will be discussed, with a view to improving our understanding of uta transmission and generating hypothese to be tested in complementary analytic studies.

B.1. House Characteristics

Stone walls were a risk factor for uta, possibly because they provide resting places for sandflies. Incompletely pointed stone walls are a characteristic of traditional houses in rural areas (Figure 16). Obviously walls of this kind have numerous holes and cracks both inside and outside and within these holes daytime temperature and humidity are suitable for sandflies. The same argument would apply to un-faced walls (significant in the matched analysis, but not by MVA). There was no any evidence that adobe or brick walls could be risk factors, possibly because both have a smooth surface. As already mentioned, stone walls were not a risk factor in region 2 because no house in this region was built with stone (Table C.I.1).

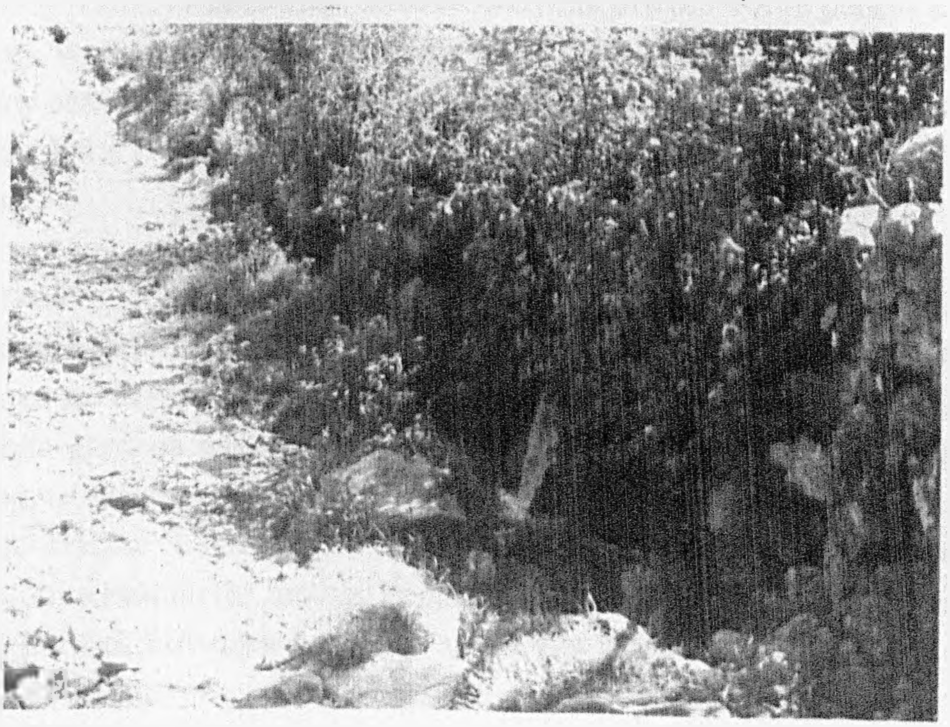
Having a cement floor has been reported as protective in Acosta, Costa Rica (Rojas-Ocampo 1993). We obtained the same result in region 2. This factor is probably a marker and not causal. Houses with finished floors are generally built with modern materials. Unfinished, earth floors are typical of houses inhabited by the poorest people. It is quite difficult to believe that earth floors provide e.g. resting places for the vector though they might affect indoor temperature and humidity. Because earth floors were a risk factor in region 2, despite similar frequencies in both regions (Figure 9) other factors are probably involved. It is unclear whether this factor implies transmission indoors or outdoors.

Holes in bedroom windows are points of entry for sandflies. This factor was not significant by region in MVA because of the small sample size (Figure 9), but its MOR in region 1 was 6.3 (c.i.: 0.75-53.6). Despite the lack of statistical significance, this is a biologically plausible risk factor. Access of the vector to houses needs to be considered in intervention programs in both region 1 and region 2. Related variables such as the total number of windows in a house, and whether windows are holed or open, are also potentially important according to matched analysis (Table B.I.1).

Herrer (1956) pointed out that smoke in houses is an irritant to sandflies. This fact is well-known by the inhabitants of some endemic areas, and they produce smoke in their houses during the periods when sandfly

Figure 16. Typical Stone Wall

Figure 17. Typical Waterway



densities are highest. In houses without chimneys the smoke repels sandflies, though the effect is temporary.

Smoke in houses as a protective factor and holes in bedrooms windows as a risk factor are further evidence for indoor transmission in region 1.

B.2. Features Around the House

In rural areas, roads are synonymous with progress and have been demonstrated to produce important ecological changes affecting flora and fauna. In towns, such as those in Sondor or Canchaque regions, where the unpaved roads were still used mainly as horseback pathways, roads gave no protection. In contrast, in some areas (Buenaventura and Arahuay regions) where paved roads are used by trucks the effect was evident. When we collected the information this variable was not stratified by type of traffic.

Having a house far from a river increased the incidence of uta. In other words, a river protected the houses located close it. This was a surprising result. Conceivably, sites close rivers are too wet to permit sandfly breeding. We have observed a decline in the abundance of sandflies during the rainy season. This effect of rivers was only observed in region 2 because in region 1 the rivers run in deep canyons and houses are rarely built close to them.

Houses without kitchen gardens had a greater OR; the kitchen gardens were a protective factor. One possible reason is the use of insecticide in kitchen gardens. Possibly this was a risk factor in region 1 only because: (i) kitchen gardens were significantly more common in this region (Figure 12), and/or (ii) people in region 2 do not use insecticide in their kitchen gardens, and/or (iii) there are differences in the types of crops between regions. This risk factor further supports the view that transmission occurs around houses, but does not allow us to say whether it occurs indoors or outdoors.

The presence of a neighbouring kitchen garden represents an increment in the area of crops around a house, and as a consequence could increase the abundance of vector in region 2, where people did not use insecticide. Kitchen gardens could be breeding and/or resting places and/or sources of sugar.

B.3. Human Indoor Behaviour

The number of residents per household (NRH) has been reported as a risk factor for CL by Van der Linden *et al.* (submitted). A significant OR for NRH essentially means the risk for any susceptible person is greater in larger families. An hypothesis to explain this risk factor is that transmission rates varies with family size. This has been observed in some infectious diseases (Anderson & May 1992), but not in vector-borne diseases. The following observations could support this hypothesis: (i) in our study areas, large families reflect a large number of children, (ii) data from Purisima region show that incidence rate of uta in unscarred children was 5.6 times higher than unscarred adults (Llanos-Cuentas, unpublished information). Thus, these age-specific differences suggest differences in the forces of infection between children and adults (Anderson & May 1992, pp.304-318). But, in a complex disease such as leishmaniasis with great heterogeneities other factors could be involved (see above). We as not know why NRH was a risk factor only in region 1. Different behaviour of the vector between regions 1 and 2 could be an alternative explanation.

Rojas *et al.* (1988), in their preliminary analysis of CL in Acosta, reported 'poor illumination' (houses with candles vs electric lights) as a potential risk factor OR = 2.7 (c.i.: 0.4-13.6, p = 0.42). Small sample size and/or the existence of confounders probably explain the lack of significance in their study. The light of lamps attracts phototropic vector species (Lewis 1971), which could explain why illumination at night was a risk factor in region 1. Proprietary kerosene lamps produce higher intensity light than home-made kerosene lamps because smoke darkens the glass of the latter. Home-made lamps may be less attractive to sandflies (OR was significant in matched analysis but not in MVA). We may remark that 5/8 individuals that used 'Petromax' lamps (which generate highest light) were affected by uta. Illumination at night was not important in region 2, where the use of proprietary lamps was more common. This suggests that the vector in this region is no phototropic and/or endophilic. In contrast, the strength of illumination as a risk factor in region 1 implies that the vector enters houses and transmission occurs indoors. Recently, it has been observed that *Lutzomyia trapidoi* in Ecuador is or is not attracted by artificial light in two areas separated by 80 kilometers (Dujardin *et al.* 1993) and the authors suggested regionally different behaviour of populations of that species.

Stored wood in houses probably provides resting places for sandflies. As its frequency was very low (Figure 10), it was detected as a significant risk factor in the pooled data only, but matched analysis pointed to its importance in region 1.

The presence of stored grain in houses was significant protective factor. Health promoters (inhabitants in endemic areas) have pointed out that people spray insecticide on these grains to deter rodents. Storing grain is a seasonal activity more common between August to December, the period of low transmission. This could explain its relatively low OR (1.77).

Domestic animals have been reported as risk factors associated with the transmission of CL by Rojas-Ocampo (1993) and by Van der Linden *et al.* (submitted). Which species are risk factors depends on vector preference. In Costa Rica, the sandfly species responsible for transmission are attracted by pigs. In region 2, the presence cows around houses was a risk factor. The role of domestic animals in relation with transmission (for OR's > 1) is to attract sandflies, or to increase population size (more blood meals or more breeding sites). Domestic animals were the main sources of vector blood meals in a recent study carried out in Chaute, Peru (Perez *et al.* 1992). In addition, the activity of cows could influence the abundance of sandfly breeding sites. The evaluation of risk due to domestic animals is problematic, because the number of animals, their distance from the house, and the number of days around the house all vary, e.g. because of restricted pasture for animals in Andean valleys, owners frequently move their animals (total or partial) to different places. Similarly, dogs, despite the common claim that they sleep outdoors frequently rest inside the house or around it during the peak of sandfly activity. Thus, we do not claim to have identified the full role of domestic animals in uta transmission. Further studies designed adequately to measure the behaviour and abundance of domestic animals should be carried out. The roles of cows and goats should be further explored in region 2, sheep in region 1, and dogs and cats in both regions.

Modification of the house (OR=1.89) was found to be a significant factor ($p < 0.05$) in matched analysis. In spite of this factor losing its significance during MVA, it has some biological plausibility. Regardless of the kind of modification made to a house, modifications temporarily allow easier access to the vector.Lane & Al-Taqui (1983), Lane (1986) and Beier *et al.* (1986) have all suggested possible associations between sandflies, building construction and increases in the incidence of leishmaniasis in Kuwait and Egypt.

B.4. Human Outdoor Behavoiur

Waterways are small channels frequently used to irrigate crops. They usually carry water for just a few hours per week. They may be associated with breeding and/or resting places for sandflies (Figure 17). Sites close to channels have low temperature, moderate humidity, and enough flora and fauna to suggest an adequate habitat for these insects.

Cutting wood probably increases the risk of subjects to sandfly bites because dry wood provides good resting places for *Lutzomyia*. This activity is twice frequent in adults as in children. Despite its higher frequency in region 2 (Figure 10, Table C.IV.1) this factor was significant only in region 1. This suggests that other factors are involved, i.e. differences in behaviour of the vector (e.g. it does not use wood as resting sites).

Irrigating crops at night is an activity likely to increase the risk of exposure to vector bites. Adults were more affected because they were more exposed (Figure 15). The different results for region 1 obtained in matched analysis by contrast with MVA could be explained by interactions with others factors which were removed through MVA. This does not exclude the possibility that this variable is a potential risk factor in region 1, and its importance should be explored in future studies.

The OR's for cutting wood (region 1), irrigation work at night (region 2) and repairing waterways (pooled data) constitute the first evidence for transmission outside homes. This finding contrasts with the textbook view that the transmission of uta occurs indoors only (Shaw & Lainson 1987, WHO 1984). Thus, indoor and outdoor transmission occur simultaneously in region 1, and possibly in 2.

B.5. Variation by Age

Whilst children and adults were subjected to markedly different rates of exposure to some variables (Figure 15), and whilst matched analysis pointed to some risk for children but not for adults (Tables D.IV.1 and D.IV.2), the definitive multivariate analysis found no evidence for age-dependent or age-modified risk.

There are no obvious reasons why the response to exposures should depend on age. In model 1, although age was a statistically significant modifier in some instances, OR's were always very close to 1 (Table E.I.3). For models 2 and 3, strikingly, the addition of interactions for age had no effect on statistics whatsoever (compare Tables E.II.2 and E.III.2 with E.II.1 and E.III.1).

B.6. Heterogeneity of risk factors

Distinct risk factors have been reported in Colombia (Weigle *et al.* 1992) and Costa Rica (Rojas *et al.* 1992, Rojas-Ocampo 1993). In both regions the similarity is that the disease is caused mainly by *L.panamensis* (Weigle *et al.* 1986, 1992, Herrero *et al.* 1992). The differences are: (i) the transmission patterns are quite different, in the jungle in Tumaco (Colombia) and apparently inside houses in Acosta (Costa Rica), and (ii) the distribution of the disease by age and sex differs (generally adults males were affected in Tumaco and children of both sexes in Acosta). In contrast, our analysis shown that risk factors vary regionally for a single *Leishmania* species (*L.peruviana*).

C. Population Attributable Risk

PAR gives the expected reduction in disease burden following removal of the study factor in question (Schlesselman 1982, Kirkwood 1988). Its magnitude depends on the proportion of a population exposed to a factor and the relative risk associated with that factor. PAR can be used to suggest interventions, set regulations, and it has been used in lawsuits concerning hazardous exposures (Greenland & Robins 1988). PAR is known by many names, population attributable risk per cent (Cole & MacMahon 1971), etiological fraction (Miettinen 1974, Schlesselman 1982), attributable risk (Breslow & Day 1980), population proportional attributable risk (Kirkwood 1988). A conceptual review and interpretation of these terms has been made by Greenland & Robins (1988). In this dissertation we use the term population attributable risk (PAR) as analogous to the concept of excess fraction defined by Greenland & Robins (1988) and calculated with formulae given by Bruzzi *et al.* (1985).

When PAR is computed for a single risk factor, without regard to other factors, the sum of a series of PAR's may exceed unity. Risk estimates may then be difficult to interpret. Several approaches have been tested to resolve this problem (Whittemore 1983, Walter 1978, 1980) including the multivariate approach (Deubner *et al.* 1980, Walter 1983). The main difficulty arises from the need to know the disease risk associated with each possible combination of exposures, and also the distribution of these factors in the population. Bruzzi *et al.* (1985) developed a straightforward approach for estimating the PAR for an individual factor subset of factors that is simultaneously adjusted for the risk attributable to the remaining factors included in the model. He emphasized that, given estimates of relative risk through MVA, PAR can be calculated using the distribution of factors among the cases only. This approach can be used in pair-matched case control studies (Bruzzi *et al.* 1985).

The goal of intervention program should be to select factors with high PAR's, that is factors with high OR's and high frequency in the target population. We selected only risk factors associated with transmission inside houses in region 1 (Table F.I.1) because they suggest options for intervention, for instance, by spraying insecticide indoors. None of the risk factors for region 2 is easily associated with a method control. The combined PAR for region 1 was as high as 0.792, which implies that removal of the three factors listed would lead to a 79.2% reduction in uta incidence.

We need to be cautious about the interpretation of PAR because current methods of calculation provide no confidence limits. However, our results suggest that preventing transmission indoors, either by repelling sandflies or killing them, ought be a successful method of control. We draw this conclusion from results obtained in region 1, but it may equally apply to region 2.

In retrospect, it is not surprising that the DDT campaign began in Peru in the 1950's had a major impact on uta incidence while it lasted (Davies *et al.*, submitted). What is now needed for uta control in Peru is a sustainable, modern equivalent. Recent successes against mosquitos obtained with pyrethroid-impregnated fabrics and curtains (e.g. Curtis *et al.* 1992) may have some lessons for sandly control too.

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Appendix 1. The case-control questionnaire for risk factors of uta.

ESTUDIO CASO CONTROL Fecha___/___/___
(dd/mm/aa)

Caso ___ Control ____ Entrevistador.............. Hora: ....

Ficha No. .... Código de la casa........... Altitud.........

Identificación...
Ap. paterno Ap. Materno Nombres

Fecha Nac. ____/___/___ Sexo: M__ F__ Raza ____ Religión_____
(dd/mm/aa)

Lugar nacimiento ....
Comunidad Distrito Provincia Depto

Lugar de residencia..
Comunidad Distrito Provincia Depto

Tiempo de residencia en casa actual ____ años ____ meses

Migraciones último año:

Fecha (dd/mm/aa)	Lugar (Comunidad Distrito)	Tiempo de estancia	Lugar endémico en Uta
....	....	....	....
....	....	....	....
....	....	....	....
....	....	....	....

Características de la casa

Edad de la casa _____ años

Situada próxima a carretera: si___ no___ Distancia _______ m

Ha realizado alguna modificación de la casa el último año:si__ no __

Acción	Si	No	Epoca (mes/año)
Aumento del número de cuartos.....	....	....	....
Ampliación de cuartos..............	....	....	....
Construído paredes nuevas..........	....	....	....
Otro (especificar).................	....	....	....

Ha fumigado su casa el último año: si___ no___ Fecha ___/___
(mm/aa)

Tiempo (años) que la familia vive en la casa:
Menor 1__ 1-4 ___ 5-9 ____ 10-14 ____ 15-19____ mayor 20 ____

Número de residentes: ______ No. permantes _____ No. temporales____

Número de pisos: _____ Número de cuartos: ______

Número de dormitorios: _____ Tamaño dormitorios: (1) ______ m^2 (2) ______ m^2 (3) ______ m^2

Tipo de piso:

tierra (1)
cemento (2)
madera (3)
otro (4)
....

Tipo de pared:

piedra (1)
abode (2)
madera (3)
ladrillo (4)
otro (5)
....

Tipo de techo:

teja (1)
calamina (2)
paja (3)
madera (4)
otro (5)
....

Cubierta de las paredes:

barro (1)
yeso (2)
cemento (3)
otro (4)
....

No. total de ventanas: _____ No. ventanas usulmente abiertas: _____

Ventanas	dormitorio(s)	resto de casa
Cubiertas por: (a)..	....	....
Area total (cm^2)...	....	....

Códigos (a): vidrio(1) madera(2) plástico(3) cartón(4) nada(5) otro(6).........

Illuminación de la casa: (a) diurna: oscura(1) clara(2) muy clara(3)
(b) nocturna: velas (1)..número____ mechero (2)..número____
petromax (3)..número____ eléctrica (4)..número____
otro (5)..número____

Localización de la cocina: dentro(1) fuera(2) distancia:_____ m

Tiene orificio por donde escapa el humo: si ____ no ____

Tipo de cocina: leña(1) carbón(2) kerosene(3) gas(4) otro(5)....

Letrina: si___ no___ distancia: ______ m

Guardan productos dentro la casa: si____ no____ donde:.........

Cuáles: semillas (1) código .... granos (2) código ....
tuberculos (3) código .... frutas (4) código ....
madera (5) código .... lana (6) código ....
cueros (7) código .... otro (8)..................

Códigos

Semillas:	Granos:	Tuberculos:	Frutas:	Madera:	Cueros:
S1 garbanzo	G1 maiz	T1 papa	F1 manzana	M1 molle	C1 vacuno

S2 frejol G2 trigo T2 yuca
S3 lenteja G3 cebada T3 camote
S4 habas G4 ...... T4 ......
S5 pallares G5 ..... T5 ......
S6 arvejas

F2 palta M2 sauce C2 caprino
F3 naranja M3 huarango C3 porcino
F4 lima M4 pajarobobo C4 .....
F5 pacae M5 .... C5 ......
F6 lima
F7 tuna
F8 granadilla
F9 chirimoya
F10........

Presencia de animales en la casa:

Especie	Donde duerme ?			Número animales	Distancia (m)
	dentro casa	corral	libre		
....	....	......	.....	....	....
....	....	......	.....	....	....
....	....	......	.....	....	....

Características alrededor de la casa:

Variable	cercanía al:		distancia (m)
	Si	No	
cerro....................	....	....	....
quebrada.................	....	....	....
carretera................	....	....	....
fuente de agua			
. rio	....	....	....
. canal	....	....	....
refugios temporales	....	....	....

Tiene huerto: si___ no___ distancia (m):___________

Tiene huerto el vecino: si ____ no ____ distancia (m): ___________

Tipo de plantas que cultiva en su huerto o existe en el huerto vecino:

....
....
....

La casa tiene pircas: si____ no___ distancia(m):__________

Extensión total de las pircas (m^2) que delimitan la huerta o división de la casa con la adyacente :

Menor 10__ 10-50 ____ 50.1-100 ____ 100.1-200 ____ 200.1-300_____
300.1 - 400 ____ 400.1-500____ mayor 500 ____

Edad de las pircas (años):
(1) menor 1 (2) 1-4 (3) 5-10 (4) mayor 10

Vegetación natural alrededor de la casa:

mitos (1) pitajaya (2) eucaliptos (3) pinos (4)
otro (5)............ otro (6).................

Actividades fuera de la casa:

Ocupación:

Agricultor (1)	Empleado (4)	Escolar (7)
Ganadería (2)	Obrero (5)	Acompañante (8)
Profesional (3)	Ama de casa (6)	Otro (9).........

Donde tiene localizada su(s) chacras	Tipo de cultivo	Epoca del año cosecha	Durmieron en la charcra:		No.visitas =< 3 meses
			caso/control	familia	
.. ..	....	....	....	......	.....
....	....	....	....	......	.....
....	....	....	....	......	.....
....	....	....	....	......	.....
....	....	....	....	......	.....
....	....	....	....	......	.....

Tiene refugios temporales en todas sus chacras: si____ no______

Tiene refugios temporales en la chacra que supuestamente se contagio:
si____ no______

Actividades desarrolladas durante los últimos 6 meses:

Actividad	No.veces	Lugar	Fecha última vez
1. reparar canales de agua	....	....	....
2. arreglar carreteras	....	....	....
3. construcción de pircas	....	....	....
4. desmatamiento	....	....	....
5. tala de árboles	....	....	....
6. regar chacra noche	....	....	....
	....	....	....

FICHA COMPLEMENTARIA CASO-CONTROL

CASO		CONTROL		Cod. casa		No.	

ACTIVIDADES FUERA DE LA CASA

Ocupación: Agricultor ( ) Ganadero ( ) Empleado ( ) Acompañante ( )
Escolar ( ) Profesional ( ) Obrero ( ) Ama-casa ( )
Otro ( )

Donde tiene localizada su(s) chacra(s):

	Identificación Chacra	Código (a)	Distancia (b)	Ubicación (c)	Caract. chacra	Durmió C/Crl	Durmió Fam	# día < 3 M
1								
2								
3								
4								
5								
6								

(a) **Código:** 1. Dentro de la comunidad, 2. Fuera de la comunidad
(b) **Distancia:** de su casa a la chacra, en tiempo caminando **en minutos.**
(c) **Ubicación:** 1. Quebrada 2. Ladera 3. Otro
(d) **Características chacra:** 1. Arboles 2. Río 3. Canal 4. Manantial (puquial) 5. Pozo 6. Otro

Para cada chacra completar la siguiente información:
(e) **Actividad :** 1= regar 2= preparar tierra 3= siembra 4= cultivar 5= cosechar 6= otro
Fumigar : 1= Si 2 = No 3 = No se sabe

Chacra 1				
Cultivo Nombre	Activ (e)	Fumigar	Meses de	Meses a

Chacra 2				
Cultivo Nombre	Activ (e)	Fumigar	Meses de	Meses a

Chacra 3				
Cultivo Nombre	Activ (e)	Fumi gar	Meses de	a

Chacra 4				
Cultivo Nombre	Activ (e)	Fumi gar	Meses de	a

Chacra 5				
Cultivo Nombre	Activ (e)	Fumi gar	Meses de	a

Chacra 6				
Cultivo Nombre	Activ (e)	Fumi gar	Meses de	a

Chacra 7				
Cultivo Nombre	Activ (e)	Fumi gar	Meses de	a

Chacra 8				
Cultivo Nombre	Activ (e)	Fumi gar	Meses de	a

Appendix 2. Epidemiological Record by Family

Distrito:.. Comunidad: .... Codigo de la casa: .... Altitud:.............

Jefe de familia...............................

					Entrevistador Fecha: / /		Entrevistador Fecha: / /		Entrevistador Fecha: / /		Entrevistador Fecha: / /	
Nombre y Apellido	Sexo	Fecha Nacimiento	IDRM	Uta (1) Status	Lesion Nueva	Obs.*	Lesion Nueva	Obs.	Lesion Nueva	Obs.	Lesion Nueva	Obs.

* En observacion, escribir 0 cuando la persona estuvo ausente por mas del 50% durante el periodo de observacion

(1) Anotar el numero de lesiones activas y cicatriciales, utilizando los codigos usuales, asi como el mes y ano de inicio de la lesion.

Appendix 3. Clinical Record

IMT"AVH"-UNIVERSIDAD PERUANA CAYETANO HEREDIA

PROGRAMA DE LEISHMAIASIS

CENTRO DE INVESTIGACION EN SALUD INS

CODIGO IMT [ ]   No. HH.CC. [ ]   FECHA ADMISION [ ]

IDENTIFICACION: ....
APELLIDO PATERNO   APELLIDO MATERNO   NOMBRES

FECHA DE NACIMIENTO: ..../...../.....   SEXO: [ ]   RAZA: [ ]

LUGAR DE NACIMIENTO:..
DEPARTAMENTO   PROVINCIA   DISTRITO   CASERIO—ANEXO

LUGAR DE CONTAGIO: ....
DEPARTAMENTO   PROVINCIA   DISTRITO   CASERIO—ANEXO

OCUPACION ACTUAL:

0.– Agricultor
1.– Minero
2.– Petrolero
4.– Maderero
8.– Su casa
16.– Profesional (e) ....
32.– Empleado (e) ....
64.– Otros (e) ....

ACTIVIDAD DESARROLLADA DURANTE EL CONTAGIO:

0.– Agricultura sin desbosque
1.– Agricultura con desbosque
2.– Petrolero
4.– Minería (oro)
8.– Madera
16.– Casa
32.– Pesca
64.– Otros (e) ....

TIEMPO DE RESIDENCIA EN LUGAR DE CONTAGIO [ ]

DIRECCION ACTUAL:..
DEPARTAMENTO   PROVINCIA   DISTRITO   CASERIO—ANEXO

DIRECCION FAMILIAR:..

FORMA CLINICA:

1.– Andina cutanea
2.– Andina mucosa
4.– Selvatica cutanea
8.– Selvatica mucosa

LESION CUTANEA: [ ] (Si)   [ ] (No)

DURACION ENFERMEDAD CUTANEA(Meses) [ ]

TIPO DE LESION :

1.– Ulcerativa
2.– Proliferativa
4.– Infiltrativa
8.– Nodular
16.– Cicatriz
32.– Otros (especificar) ....

TAMAÑO DE LAS LESIONES: Graficar en plástico (todos) y emgrapar en la ficha

(1) . . . .; (2) . . . . ; (3). . . . . ; (4) . . . . (5) . . . .

SI TIENE CICATRIZ : A) En que año adquirio la lesión primaria . . . .

B) Cuanto tiempo (meses) demoró en cicatrizar . . . .

C) Recibió tratamiento específico . . . . Si . . . . No.

ANTECEDENTES DE TRATAMIENTO DE LA LESION CUTANEA ACTIVA:

1.– Repodral – Total ampollas: . . . . Mes – Año : . . . .

2.– Glucantime–Total ampollas: . . . . Mes – Año : . . . .

4.– Remedio vegetal (cuál) : . . . .

8.– Quemo lesión : . . . .

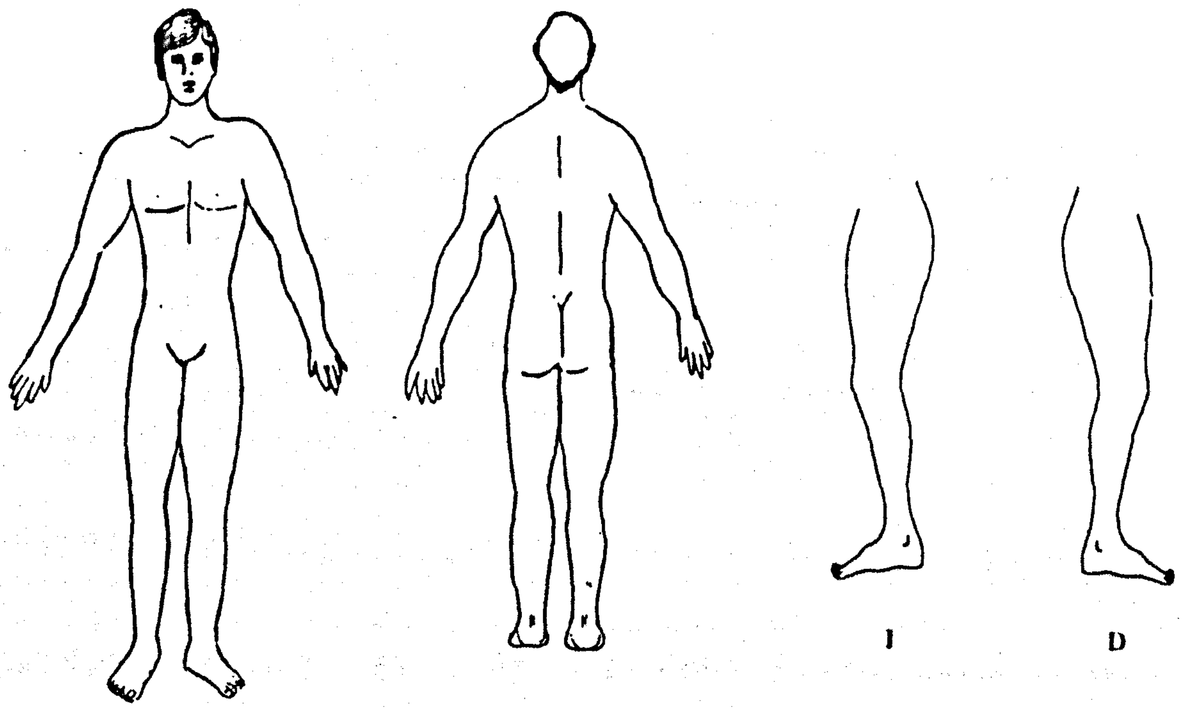
16.– No recuerda . . . .

32.– No tratamiento: . . . .

RESPUESTA AL TRATAMIENTO: 1.– Cura completa ( ) 4.– No Modificó ( )

2.– Mejoria ( ) 8.– No recuerda ( )

LOCALIZACION DE LESIONES: Grafical y diferencial las activas de las cicatrices



I D

LESION MUCOSA: SI – 1 NO – 2 Si la respuesta es SI:

DURACION DE LA ENFERMEDAD (meses) ☐

SINTOMAS:

0 – Asintomático

1 – Tupidez nasal y/o costras

2 – Obstrucción nasal permanente

4 – Disfonia leve a moderada

8 – Disfonia severa

16 – Odinofagia

32 – Distres respiratorio leve–moderado

64 – Distres respiratorio severo

128 – Otros . . . .

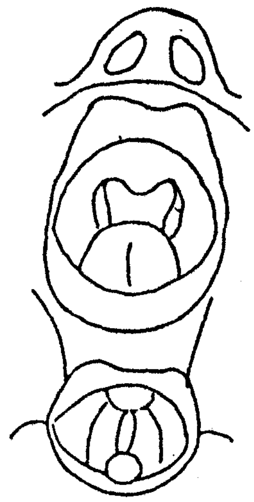
EXTENSION DEL COMPROMISO MUCOSO:

1.– NASAL : SEPTO 0 – No
1 – Infiltrado
2 – Perforado
4 – Amputado

CORNETES : 0 – No.
1 – Infiltrado
2 – Amputado

ALAS: 0 – No
1 – Infiltrado
2 – Amputado

2.– Rinofaringe
4.– Paladar y/o uvula
8.– Labio superior
16.– Laringe
32.– Labio inferior
64.– Otros ....



ANTECEDENTES DE TRATAMIENTO DE LA LESION MUCOSA: SI – 1 NO – 2

Si la respuesta es afirmativa:

1.– *Antimonial trivalente* : .... .ampollas Tiempo de .... a ....
2.– Antimonial pentavalente : .... ampollas Tiempo de .... a ....
4.– Remedio vegetal; cuál : ....
8.– Quemo lesión : ....
16.– No recuerda : ....
32.– No tratamiento: ....

Tratamiento Actual : **Peso :** ....**kg** **Talla :** ....**mts.** **PA :** .... **FC :** ....

Droga : .... **Dosis :** ....

Fecha de Inicio : | | | |

Fecha de Termino : | | | |

Efectos Colaterales : ____

____

____

DIAGNOSTICO

INMUNOLOGICOS				EXAMENES PARASITOLOGICOS									
LEISHMANINA		SEROLOGIA		DIRECTO		CULTIVO		HAMSTER		HISTOLOGIA		OTROS	
Fecha	Respuesta	Fecha	Respuesta	Fecha	Respuesta	Fecha	Respuesta	Fecha	Respuesta	Fecha	Respuesta	Fecha	Respuesta

EVOLUCION :

Appendix 4. Cross-correlation of Variables in Region 1.

Correlations:	NTOVEN	NVENAB	VDORAREA	ORIHUMO	EDCASAM	TADORM
NTOVEN	1.0000	.6057**	.3092**	.1373	-.0322	-.0451
NVENAB	.6057**	1.0000	-.1822*	.1375	.0517	-.0403
VDORAREA	.3092**	-.1822*	1.0000	.0408	-.0515	.0018
ORIHUMO	.1373	.1375	.0408	1.0000	-.1299	-.0302
EDCASAM	-.0322	.0517	-.0515	-.1299	1.0000	.0434
TADORM	-.0451	-.0403	.0018	-.0302	.0434	1.0000
DISCOSI	-.0698	-.0671	-.0173	-.1313	-.0362	-.0035
MODICAS	.1264	.0518	.0112	.0644	-.1421	-.0574
MECHERO	-.0956	-.1139	.1213	-.0903	.2344**	.0919
PETROM	.0218	.0531	-.0755	.0307	-.0482	-.0251
MADERA	.1760*	-.0581	.3362**	.1058	.0676	-.0305
NVREGAR	.3858**	.3456**	-.0647	-.0663	-.0724	-.0065
NOCHES	.0318	-.0636	-.0220	.0563	-.0302	.0052
NDIAQ	.0632	.0293	.0589	-.0455	.0004	-.0420
FLOOR	-.2051**	-.0218	-.1359	.1209	.0400	.0683
WALL	-.0425	-.0449	-.0271	.0867	.2799**	-.0615
COVERW	-.3392**	-.0627	-.2236**	-.0501	-.1659*	-.0793
CREEK	-.0609	.1482	-.1683*	.0916	-.0403	-.0592
RIVER	.1099	.1878*	-.0526	-.0727	.0778	-.0318
CHANL	-.0631	.1546*	-.1873*	.0936	-.1242	-.0225
VECIY	-.1558*	.0114	-.1389	.0244	-.1586*	-.0685
WDAB1	.1558*	.1295	.0622	-.0433	-.0200	-.0165
KERO	-.0844	-.1305	.1640*	-.1568*	.1893*	.1446
ROAD	-.1680*	-.0720	-.2047**	-.0651	-.0422	.0975

Number of cases: 237   1-tailed Signif: * - .01 ** - .001
"." is printed if a coefficient cannot be computed

continuation Appendix 4....

Correlations:	DISCOSI	MODICAS	MECHERO	PETROM	MADERA	NVREGAR
NTOVEN	-.0698	.1264	-.0956	.0218	.1760*	.3858**
NVENAB	-.0671	.0518	-.1139	.0531	-.0581	.3456**
VDORAREA	-.0173	.0112	.1213	-.0755	.3362**	-.0647
ORIHUMO	-.1313	.0644	-.0903	.0307	.1058	-.0663
EDCASAM	-.0362	-.1421	.2344**	-.0482	.0676	-.0724
TADORM	-.0035	-.0574	.0919	-.0251	-.0305	-.0065
DISCOSI	1.0000	.1374	-.0493	-.0150	-.0240	-.0293
MODICAS	.1374	1.0000	-.0774	.0134	.0502	-.0398
MECHERO	-.0493	-.0774	1.0000	-.0638	.2361**	-.0725
PETROM	-.0150	.0134	-.0638	1.0000	.2413**	-.0217
MADERA	-.0240	.0502	.2361**	.2413**	1.0000	-.0318
NVREGAR	-.0293	-.0398	-.0725	-.0217	-.0318	1.0000
NOCHES	.0445	.0899	.0181	-.0678	.0043	-.0316
NDIAQ	-.0088	.0464	.0635	-.0488	-.0537	.1294
FLOOR	-.0157	-.1012	-.0003	.0500	.0218	-.1288
WALL	.0472	.0312	.1789*	.1119	.2934**	-.0456
COVERW	.0060	-.0638	.0019	.0852	-.0857	-.1089
CREEK	-.0171	-.0067	-.2046**	.1090	-.1327	-.0633
RIVER	-.0207	.0040	.0253	.1054	-.0520	-.0261
CHANL	.0033	.1804*	-.3465**	.0610	-.1700*	-.0936
VECIY	.0618	.1211	-.1465	-.0324	-.0467	-.0697
WDAB1	-.0006	-.0118	-.0055	.2113**	.0230	-.0294
KERO	.0716	-.0492	.7446**	-.0638	.2008**	.1205
ROAD	.0884	.1245	.0099	.0207	-.0783	-.0809

Number of cases: 237 1-tailed Signif: * - .01 ** - .001
"." is printed if a coefficient cannot be computed

continuation Appendix 4....

Correlations:	NOCHES	NDIAQ	FLOOR	WALL	COVERW	CREEK
NTOVEN	.0318	.0632	-.2051**	-.0425	-.3392**	-.0609
NVENAB	-.0636	.0293	-.0218	-.0449	-.0627	.1482
VDORAREA	-.0220	.0589	-.1359	-.0271	-.2236**	-.1683*
ORIHUMO	.0563	-.0455	.1209	.0867	-.0501	.0916
EDCASAM	-.0302	.0004	.0400	.2799**	-.1659*	-.0403
TADORM	.0052	-.0420	.0683	-.0615	-.0793	-.0592
DISCOSI	.0445	-.0088	-.0157	.0472	.0060	-.0171
MODICAS	.0899	.0464	-.1012	.0312	-.0638	-.0067
MECHERO	.0181	.0635	-.0003	.1789*	.0019	-.2046**
PETROM	-.0678	-.0488	.0500	.1119	.0852	.1090
MADERA	.0043	-.0537	.0218	.2934**	-.0857	-.1327
NVREGAR	-.0316	.1294	-.1288	-.0456	-.1089	-.0633
NOCHES	1.0000	.0407	.1087	.0099	-.0697	-.0980
NDIAQ	.0407	1.0000	-.0907	-.0486	.0146	.1558*
FLOOR	.1087	-.0907	1.0000	.0151	.1311	.0216
WALL	.0099	-.0486	.0151	1.0000	.0074	-.0840
COVERW	-.0697	.0146	.1311	.0074	1.0000	.1724*
CREEK	-.0980	.1558*	.0216	-.0840	.1724*	1.0000
RIVER	-.0761	.0824	-.1494	-.0880	-.0463	.0910
CHANL	.0806	.0451	.1824*	-.2246**	.2199**	.2664**
VECIY	.0290	.0055	-.0975	-.1390	.2118**	.1675*
WDAB1	-.0252	.0510	-.0142	.0101	-.0520	.0617
KERO	-.0294	.0474	-.0414	.1081	-.0544	-.2046**
ROAD	.0429	.1261	.1330	-.1352	.1155	.1047

Number of cases: 237 1-tailed Signif: * - .01 ** - .001
"." is printed if a coefficient cannot be computed

continuation Appendix 4....

Correlations:	RIVER	CHANL	VECIY	WDAB1	KERO	ROAD
NTOVEN	.1099	-.0631	-.1558*	.1558*	-.0844	-.1680*
NVENAB	.1878*	.1546*	.0114	.1295	-.1305	-.0720
VDORAREA	-.0526	-.1873*	-.1389	.0622	.1640*	-.2047**
ORIHUMO	-.0727	.0936	.0244	-.0433	-.1568*	-.0651
EDCASAM	.0778	-.1242	-.1586*	-.0200	.1893*	-.0422
TADORM	-.0318	-.0225	-.0685	-.0165	.1446	.0975
DISCOSI	-.0207	.0033	.0618	-.0006	.0716	.0884
MODICAS	.0040	.1804*	.1211	-.0118	-.0492	.1245
MECHERO	.0253	-.3465**	-.1465	-.0055	.7446**	.0099
PETROM	.1054	.0610	-.0324	.2113**	-.0638	.0207
MADERA	-.0520	-.1700*	-.0467	.0230	.2008**	-.0783
NVREGAR	-.0261	-.0936	-.0697	-.0294	.1205	-.0809
NOCHES	-.0761	.0806	.0290	-.0252	-.0294	.0429
NDIAQ	.0824	.0451	.0055	.0510	.0474	.1261
FLOOR	-.1494	.1824*	-.0975	-.0142	-.0414	.1330
WALL	-.0880	-.2246**	-.1390	.0101	.1081	-.1352
COVERW	-.0463	.2199**	.2118**	-.0520	-.0544	.1155
CREEK	.0910	.2664**	.1675*	.0617	-.2046**	.1047
RIVER	1.0000	-.0619	.0963	.1932*	.0253	-.0469
CHANL	-.0619	1.0000	.4009**	-.1432	-.3465**	.1835*
VECIY	.0963	.4009**	1.0000	-.1194	-.1276	-.0549
WDAB1	.1932*	-.1432	-.1194	1.0000	.0398	.1428
KERO	.0253	-.3465**	-.1276	.0398	1.0000	-.0467
ROAD	-.0469	.1835*	-.0549	.1428	-.0467	1.0000

Number of cases: 237   1-tailed Signif: * - .01 ** - .001
"." is printed if a coefficient cannot be computed

Appendix 5. Cross-correlation of Variables in Region 2.

Correlations:	NTOVEN	NVENAB	VDORAREA	ORIHUMO	EDCASAM	TADORM
NTOVEN	1.0000	.5573**	.6171**	.0270	.0566	.1762*
NVENAB	.5573**	1.0000	.0431	.0511	-.1249	.0131
VDORAREA	.6171**	.0431	1.0000	-.0276	.1184	.1876**
ORIHUMO	.0270	.0511	-.0276	1.0000	-.0836	-.0267
EDCASAM	.0566	-.1249	.1184	-.0836	1.0000	.2031**
TADORM	.1762*	.0131	.1876**	-.0267	.2031**	1.0000
DISCOSI	.0769	-.0683	.1168	.0060	.0461	-.0838
MODICAS	.0143	.1067	.0108	.1034	-.1876**	-.1295
MECHERO	-.1693*	-.0741	-.1871**	-.0485	-.0138	-.0940
PETROM	.	.	.	.	.	.
MADERA	.0435	.1134	-.0685	.0370	-.0554	-.0805
NVREGAR	.0752	.0943	.0343	-.1084	.2490**	.0429
NOCHES	.0918	.1223	.0668	.0389	.0045	.0874
NDIAQ	-.0413	-.0380	.0430	.0229	.0767	.0862
FLOOR	-.3452**	-.3030**	-.2904**	.2017**	-.0727	-.0453
WALL	.	.	.	.	.	.
COVERW	-.1823*	-.1439*	-.1815*	.1316	-.0636	-.1159
CREEK	.1301	.0558	-.0701	.0554	.0304	-.1295
RIVER	.1154	-.0973	.1747*	-.0453	.1324	.0609
CHANL	-.1364	.0065	-.1064	.0082	-.0140	-.0488
VECIY	.0023	.0751	.0079	.0595	-.1094	.0415
WDAB1	.3182**	.2872**	.2272**	.1467*	.0288	.2016**
KERO	-.2944**	.0060	-.2424**	-.0038	-.0151	-.0687
ROAD	-.2437**	-.0782	-.3055**	.0023	-.0463	-.0710

Number of cases: 283 1-tailed Signif: * - .01 ** - .001
". " is printed if a coefficient cannot be computed

continuation Appendix 5....

Correlations:	DISCOSI	MODICAS	MECHERO	PETROM	MADERA	NVREGAR
NTOVEN	.0769	.0143	-.1693*	.	.0435	.0752
NVENAB	-.0683	.1067	-.0741	.	.1134	.0943
VDORAREA	.1168	.0108	-.1871**	.	-.0685	.0343
ORIHUMO	.0060	.1034	-.0485	.	.0370	-.1084
EDCASAM	.0461	-.1876**	-.0138	.	-.0554	.2490**
TADORM	-.0838	-.1295	-.0940	.	-.0805	.0429
DISCOSI	1.0000	.1060	-.0180	.	-.0108	.0022
MODICAS	.1060	1.0000	-.0778	.	.1019	-.0329
MECHERO	-.0180	-.0778	1.0000	.	.1296	-.1085
PETROM	.	.	.	1.0000	.	.
MADERA	-.0108	.1019	.1296	.	1.0000	-.0355
NVREGAR	.0022	-.0329	-.1085	.	-.0355	1.0000
NOCHES	-.0074	-.0562	.0037	.	-.0800	.2627**
NDIAQ	-.0022	.0397	.0303	.	.1320	.0313
FLOOR	.0655	.0626	.1713*	.	.0180	-.0448
WALL	.	.	.	.	.	.
COVERW	.0548	.0454	.2003**	.	-.0250	-.1217
CREEK	-.0531	.0153	.0121	.	.1251	-.0480
RIVER	-.0681	-.0906	.0988	.	-.0972	-.0478
CHANL	.1119	.1000	-.1218	.	.0322	.1587*
VECIY	.0607	.2387**	-.0328	.	.0995	-.0628
WDAB1	.0871	.1655*	-.1069	.	-.0156	-.0033
KERO	-.0770	.0283	.6533**	.	.1048	-.0906
ROAD	.0485	.0131	.0671	.	.0653	-.0404

Number of cases: 283 1-tailed Signif: * - .01 ** - .001
". " is printed if a coefficient cannot be computed

continuation Appendix 5....

Correlations:	NOCHES	NDIAQ	FLOOR	WALL	COVERW	CREEK
NTOVEN	.0918	-.0413	-.3452**	.	-.1823*	.1301
NVENAB	.1223	-.0380	-.3030**	.	-.1439*	.0558
VDORAREA	.0668	.0430	-.2904**	.	-.1815*	-.0701
ORIHUMO	.0389	.0229	.2017**	.	.1316	.0554
EDCASAM	.0045	.0767	-.0727	.	-.0636	.0304
TADORM	.0874	.0862	-.0453	.	-.1159	-.1295
DISCOSI	-.0074	-.0022	.0655	.	.0548	-.0531
MODICAS	-.0562	.0397	.0626	.	.0454	.0153
MECHERO	.0037	.0303	.1713*	.	.2003**	.0121
PETROM	.	.	.	.	.	.
MADERA	-.0800	.1320	.0180	.	-.0250	.1251
NVREGAR	.2627**	.0313	-.0448	.	-.1217	-.0480
NOCHES	1.0000	.0108	-.0179	.	-.0312	-.1637*
NDIAQ	.0108	1.0000	.0254	.	.0642	.0033
FLOOR	-.0179	.0254	1.0000	.	.2970**	.0798
WALL	.	.	.	1.0000	.	.
COVERW	-.0312	.0642	.2970**	.	1.0000	.1207
CREEK	-.1637*	.0033	.0798	.	.1207	1.0000
RIVER	-.1050	-.0861	-.1652*	.	.1864**	-.0271
CHANL	.0411	-.0103	.1904**	.	.0129	.0713
VECIY	-.0960	-.0313	.1508*	.	-.0539	.0288
WDAB1	.0999	.0111	-.0831	.	.0686	-.1345
KERO	.0500	.1105	.2286**	.	.1373	-.0579
ROAD	.0290	.0552	.3894**	.	.1786*	.0989

Number of cases: 283 1-tailed Signif: * - .01 ** - .001
". " is printed if a coefficient cannot be computed

continuation Appendix 5....

Correlations:	RIVER	CHANL	VECIY	WDAB1	KERO	ROAD
NTOVEN	.1154	-.1364	.0023	.3182**	-.2944**	-.2437**
NVENAB	-.0973	.0065	.0751	.2872**	.0060	-.0782
VDORAREA	.1747*	-.1064	.0079	.2272**	-.2424**	-.3055**
ORIHUMO	-.0453	.0082	.0595	.1467*	-.0038	.0023
EDCASAM	.1324	-.0140	-.1094	.0288	-.0151	-.0463
TADORM	.0609	-.0488	.0415	.2016**	-.0687	-.0710
DISCOSI	-.0681	.1119	.0607	.0871	-.0770	.0485
MODICAS	-.0906	.1000	.2387**	.1655*	.0283	.0131
MECHERO	.0988	-.1218	-.0328	-.1069	.6533**	.0671
PETROM	.	.	.	.	.	.
MADERA	-.0972	.0322	.0995	-.0156	.1048	.0653
NVREGAR	-.0478	.1587*	-.0628	-.0033	-.0906	-.0404
NOCHES	-.1050	.0411	-.0960	.0999	.0500	.0290
NDIAQ	-.0861	-.0103	-.0313	.0111	.1105	.0552
FLOOR	-.1652*	.1904**	.1508*	-.0831	.2286**	.3894**
WALL	.	.	.	.	.	.
COVERW	.1864**	.0129	-.0539	.0686	.1373	.1786*
CREEK	-.0271	.0713	.0288	-.1345	-.0579	.0989
RIVER	1.0000	-.3939**	-.1830**	.0952	-.0971	-.2475**
CHANL	-.3939**	1.0000	.2548**	.0428	.0125	.2190**
VECIY	-.1830**	.2548**	1.0000	-.0803	.0544	.0052
WDAB1	.0952	.0428	-.0803	1.0000	-.0203	-.0754
KERO	-.0971	.0125	.0544	-.0203	1.0000	.1682*
ROAD	-.2475**	.2190**	.0052	-.0754	.1682*	1.0000

Number of cases: 283 1-tailed Signif: * - .01 ** - .001
". " is printed if a coefficient cannot be computed

Appendix 6. Estimation of Population Attributable Risk for Three Selected Factors in Region 1
Case-Control Study on Cutaneous Leishmaniasis, Peru 1991-1992

to	0	1	1	1							
var	1	2	3	4					all		2
j		ORI	KERO	WALL	NCAS	NCON	p(j)	R(j)	p/R	i-0	ORI
0	0	0	0	0	7	13	7.8%	1.000	0.078	0	0.078
1	0	0	0	1	3	0	3.3%	4.100	0.008	1	0.033
2	0	0	1	0	4	21	4.4%	2.927	0.015	2	0.044
3	0	0	1	1	0	3	0.0%	12.001	0.000	3	0.000
4	0	1	0	0	15	21	16.7%	3.387	0.049	0	0.049
5	0	1	0	1	13	2	14.4%	13.888	0.010	1	0.043
6	0	1	1	0	40	73	44.4%	9.915	0.045	2	0.131
7	0	1	1	1	8	14	8.9%	40.650	0.002	3	0.026
Sum					90	147	100.0%		0.208		0.405
B	0.0	1.22	1.07	1.41			EF (ARc) =		0.792		0.595
SE(B)	0.00	0.43	0.53	0.49							
OR	1.00	3.39	2.93	4.10							

Ref: Bruzzi, P. et al. (1985). Am. J. Epidemiol., 122, 904-14.